Duration of antibacterial treatment for uncomplicated urinary tract infection in women (Review)

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ABSTRACT

Background
Uncomplicated urinary tract infection (UTI) is a common disease, occurring frequently in young sexually active women. In the past, seven day antibiotic therapy was recommended while the current practice is to treat uncomplicated UTI for three days.

Objectives
TO compare the efficacy and safety of three-day antibiotic therapy to multi-day therapy (five days or longer) on relief of symptoms and bacteriuria at short-term and long-term follow-up.

Search strategy
The Cochrane Library (Issue 1, 2004), the Cochrane Renal Group's Register of trials (July 2003), EMBASE (January 1980 to August 2003), and MEDLINE (January 1966 to August 2003) were searched. We scanned references of all included studies and contacted the first or corresponding author of included trials and the pharmaceutical companies.

Selection criteria
Randomised controlled trials comparing three-days oral antibiotic therapy with multi-day therapy (five days and longer) for uncomplicated cystitis in 18 to 65 years old non-pregnant women without signs of upper UTI.

Data collection and analysis
Data concerning bacteriological and symptomatic failure rates, occurrence of pyelonephritis and adverse effects were extracted independently by two reviewers. Relative risk (RR) and their 95% confidence intervals (CI) were estimated. Outcomes were also extracted by intention-to-treat analysis whenever possible.

Main results
Thirty-two trials (9605 patients) were included. For symptomatic failure rates, no difference between three-day and 5-10 day antibiotic regimen was seen short-term (RR 1.06, 95% CI 0.88 to 1.28) and long-term follow-up (RR 1.09, 95% CI 0.94 to 1.27). Comparison of the bacteriological failure rates showed that three-day therapy was less effective than 5-10 day therapy for the short-term follow-up, however this difference was observed only in the subgroup of trials that used the same antibiotic in the two treatment arms (RR 1.37, 95% CI 1.07 to 1.74, P = 0.01). This difference was more significant at long-term follow-up (RR 1.43, 95% CI 1.19 to 1.73, P = 0.0002). Adverse effects were significantly more common in the 5-10 day treatment group (RR 0.83, 95% CI 0.74 to 0.93, P = 0.0010). Results were consistent for subgroup and sensitivity analyses.

Authors' conclusions
Three days of antibiotic therapy is similar to 5-10 days in achieving symptomatic cure during uncomplicated UTI treatment, while the longer treatment is more effective in obtaining bacteriological cure. In spite of the higher rate of adverse effects, treatment for 5-10 days could be considered for treatment of women in whom eradication of bacteriuria is important.

PLAIN LANGUAGE SUMMARY

Uncomplicated urinary tract infection (UTI) is a common disease occurring frequently in young women. It is caused by bacteria multiplying in urine, and the patient usually complains of urgency and burning pain while urinating. The present practice is to treat the patient with antibiotics for three days. In this review we included all studies that compared three-day therapy with longer treatment (five days or more). Three days of treatment were adequate to achieve symptomatic relief for most patients, but it appears that longer therapy is better in terms of bacteria elimination from the urine, no matter what antibiotic is used. Longer therapy for UTI is related to higher rate of adverse reactions to the antibiotics used. Pending further research, it could be considered for women in whom eradication of bacteria in the urine is important.

BACKGROUND

Uncomplicated urinary tract infection (UTI) is a common disease, occurring frequently in young sexually active women. In one cohort study the incidence of the disease was estimated to be 0.5-0.7/person-year (Hooton 1996). All over the world the most common pathogens of uncomplicated UTI are similar: 80-90% *Escherichia coli*, 5-10% *Staphylococcus saprophyticus*, the remaining infections being caused by *Proteus* spp., and other Gram-negative rods. Most are bacteria from the gut that colonize the perineum and then ascend through the urethra to infect the bladder mucosa. The infection causes specific symptoms, mainly the triad of dysuria (painful urination), urgency (the urgent need to void) and frequency (very frequent urination). In randomised controlled trials (RCTs) the diagnosis is based on positive urine cultures in symptomatic subjects. In the past, the threshold for diagnosis of UTI was $>10^5$ colony forming units (CFU)/ml of voided midstream urine (Stamm 1982). However two decades ago studies have shown that in young symptomatic women with leucocyturia even 100 CFU/ml voided midstream urine can establish the diagnosis (Stamm 1980; Stamm 1982; Kunin 1993).

A large range of antimicrobials with different rates of cure and side effects are used in the treatment of UTI. It is thought that a short-course therapy consisting of a three-day antibacterial regimen is sufficient for uncomplicated urinary tract infection, as it is probably as effective as 7-10 days therapy, and may be associated with less side effects and lower costs (Hooton 1997). Single dose therapy has been advocated for years but about a decade ago reviews have raised doubts as to its use because of a higher frequency of bacteriological recurrence (Leibovici 1991; Norrby 1990), and it is no longer common clinical practice. On the other hand, single-dose treatment probably achieves symptomatic relief more rapidly than seven days of treatment (Arav-Boger 1994).

In most clinical trials assessing effectiveness of therapy, cure was defined as bacteriological cure, rather than symptomatic relief. Uncomplicated UTI is not considered a serious disease. It is not clear whether untreated UTI can progress to pyelonephritis, and if so how often. Progression to pyelonephritis probably occurs at a very low rate, while asymptomatic bacteriuria in young, healthy and non-pregnant women is not associated with renal damage (Stamm 1991).

Thus since our last systematic review on the length of treatment of uncomplicated UTI in young women (Leibovici 1991), the following questions arose:
1. What is the relative effectiveness of three days treatment compared with multi-day treatment?
2. Is any difference modified by the antibiotic used (old versus new) or CFU/ml count?
3. Do persistent positive cultures lead to persistent symptoms?
4. What is the relative effectiveness of single dose and three-day treatment, compared with seven days treatment, when the outcome of interest is symptomatic cure rather than bacteriological one?
5. Does the duration of treatment influence the development of resistant strains during treatment?

OBJECTIVES

The main objective of this review was to assess the evidence, as found in RCTs for the relative effectiveness of different regimens of antibacterial treatments in acute, uncomplicated lower urinary tract infection in otherwise healthy 16 to 65 years old females.

Specific objectives were:
1. To assess the evidence for the relative effectiveness as assessed in RCT's comparing three-day versus multi-day therapy on:
a. Relief of symptoms within two weeks after start of treatment (mostly within seven days)
b. Resolution of bacteriuria within two weeks after start of treatment (bacteriological cure)
c. Recurrence of symptoms or bacteriuria between cure and up-to eight weeks after start of treatment
d. To assess the frequency of adverse events in the different regimens

2. To assess the evidence for the relative effectiveness of the different antibacterial drugs used in the RCTs.
3. To assess the evidence for development of resistance for different durations of treatment with different drugs (comparing resistance of grown bacteria before and after therapy).

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

We attempted to identify all RCTs comparing the relative effectiveness of three day versus five days or longer oral antibacterial therapy for uncomplicated UTI in women.

Types of participants

We included studies on ambulatory, otherwise healthy women, aged 16-65 years, with uncomplicated UTI defined by the presence of urinary complaints (and by the absence of upper UTI signs); whenever possible, analysis for the review was limited to women with positive urine cultures of more than 100 CFU/ml of voided midstream urine or obtained via urinary catheter.

Uncomplicated UTI was defined as the absence of all the following:
1. Costovertebral pain or tenderness
2. Fever (more than 37.8 C)
3. Positive blood cultures.

In addition, trials of the following groups of people were excluded from the review:
1. Multiple vomiting
2. Sepsis
3. Children up to the age of 16 years
4. Hospital acquired infection
5. Pregnancy
6. Indwelling urinary catheter
7. Recent urinary tract instrumentation
8. Known pathological, functional or anatomic abnormality of the urinary tract
9. Diabetes mellitus
10. Immunocompromised patients

Types of intervention

Three days oral antibacterial treatment versus antibacterial treatment for five days or more (antibacterial therapy given in both arms did not have to be identical).

Types of outcome measures

1. Short-term symptomatic failure, defined as persistence or recurrence of symptoms up to two weeks after starting treatment.
2. Long-term symptomatic failure, defined as persistence or recurrence of urinary symptoms up to eight weeks after start of treatment.
3. Short-term bacteriological failure, defined as a positive urine culture at the first follow-up within two weeks after start of treatment.
4. Long-term bacteriological failure, defined as a positive urine culture up to eight weeks after start of treatment.
5. Occurrence of pyelonephritis during follow-up.

6. Adverse events:

a. Any serious adverse events that are fatal, life-threatening, or requiring hospitalisation;
b. Any adverse events that result in significant disability or incapacity;
c. Any important medical events that may not be immediately life-threatening, or result in death or hospitalisation, but may jeopardize the patient or may require intervention to prevent one of the above outcomes;
d. Any adverse events that require discontinuation of medication.
e. Adverse events by the involved organs: skin, gastro-intestinal, vaginal discharge, central nervous system, others.

7. The percentage of pathogens resistant to the study drug two to eight weeks after start of treatment.

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: Cochrane Renal Group methods used in reviews.

A). *The Cochrane Library* (Issue 3, 2003), the Cochrane Renal Group's Register of trials (July 2003), EMBASE (January 1980 to August 2003), and MEDLINE (January 1966 to August 2003) were searched with the phrase:
[(urinary near infection*) or cystitis or uti] and [(treatment near duration) or (single near dos*) or (3 near day*) or (three near day*)]

We included all languages. By leaving single dose in the search strategy we found articles that include single and three-day doses versus multi-day.

B). An additional search was performed in January 2004 with the assistance of the Trials Search Coordinator (see additional Table 01 - *Electronic databases searched*)
C). Reference searching and personal contact: The references of all identified studies were inspected for more studies. Additionally, the first or corresponding author of each included study was contacted for complementary information on his own trial as needed.

METHODS OF THE REVIEW

Two reviewers independently inspected each reference identified by the search and applied the inclusion criteria. For possible relevant articles, or in cases of disagreement between the two reviewers, the full article was obtained and inspected independently by a third reviewer.

Quality assessment

Trials fulfilling the review inclusion criteria were assessed for methodological quality by two reviewers. This was done using the criteria described in the Cochrane Handbook (Clarke 1999), based on the evidence of a strong association between poor allocation

concealment and overestimation of effect (Schulz 1995) and defined as below:

Allocation concealment

A. Low risk of bias (adequate allocation concealment)
B. Moderate risk of bias (some doubt about the allocation concealment)
C. High risk of bias (inadequate allocation concealment)

For the purpose of the analyses in this review, trials were included if they meet the criteria A or B in the Handbook (Clarke 1999; Kunz 1998).

Intention-to-treat (ITT) analysis

ITT analysis was performed regarding all dropouts in study as failures to achieve symptomatic or bacteriological cure. Whenever possible, we regarded only the patients with positive urine cultures (significant bacteriuria) as the reference total patient number in the two study arms. When the numbers of randomised women with positive cultures in the study groups was unavailable, the total number of randomised patients was taken for performing the ITT analysis for symptomatic short-term and long-term failures, but not for the bacteriologic outcomes.

Data collection

Two reviewers independently extracted the data of included trials. Trials were identified by the name of the first author and year in which the trial was first published and ordered chronologically. The following data will be extracted, checked and recorded:

(i) Characteristics of trials

* Date, location, period of data collection, year of publication;
* Publication status;
* Case definitions (symptomatic, bacteriological, both)
* Bacteriologic definition (10^5 or 10^2 CFU/ml)
* Sponsor of trial (commercial, academic, pharmaceutical, or unknown)
* Blinding
* Allocation concealment (yes, no and method)
* Definitions of cure (symptomatic, bacteriological or both)

(ii) Characteristics of participants

* Number of participants in each group;
* Age (as described in the article: mean, median or range);

(iii) Characteristics of interventions

* Type, dose and duration of antibacterial therapy;

(iv) Characteristics of outcome measures

* No of patients with bacteriological cure (as defined above) in each group;
* No of patients with symptomatic recurrence (as defined above) in each group, divided into local and systemic recurrences;
* No of patients with bacteriological recurrence (as defined above) in each group;
* No of patients with adverse reactions, per type and total;
* No of patients with resistant microorganisms, as defined above;
* Lost to each follow-up (dropouts) before end of study.

Data synthesis

Dichotomous data was analysed by calculating the relative risk (RR) for each trial with the uncertainty in each result being expressed using 95% confidence intervals (CI). Whenever comparisons made between the mean duration of symptoms in the two groups were normally distributed, these continuous data were analysed by using the mean and standard deviation of each trial and calculating the effect size (average mean difference) and the 95% CI.

Heterogeneity and publication bias

Heterogeneity in the results of the trials was initially assessed by inspection of graphical presentations and by calculating a test of heterogeneity (Chi^2 and I^2 - Higgins 2003). We anticipated between-trial variation in estimation of morbidity for those patients who were treated with different antibiotics. Subgroup analyses were performed in order to assess the impact of this possible source of heterogeneity in the main results. The following factors were checked: allocation generation and concealment methods, different antibiotics groups (quinolones, beta-lactams etc), per cent of dropouts in the studies.

A funnel plot estimating the precision of trials (plots of RR for efficacy against the sample size) was examined in order to estimate potential asymmetry. A fixed effect model was used throughout the review, except in the event of significant heterogeneity between the trials ($P < 0.10$), when the random effect model was chosen.

DESCRIPTION OF STUDIES

The computerised search strategy identified a large number of publications comparing different regimens of antibiotic therapy for UTI, not all relevant for the present review. These were screened for RCTs, uncomplicated UTIs, antibiotics treatment duration and presence of exclusion criteria. Of 56 trials obtained this way 24 were excluded for different reasons (see *Table of excluded studies*) while 32 RCTs were considered eligible for this review.

Two reports were identified as duplicate publications and are considered under their primary reference (Sandberg 1985). Five publications were found to be case-control or non randomised studies (Bargelloni 1972; Furusawa 1994; Hoigne 1977; Liudvig 1996; Loran 1997), while five others were reviews of different trials of which several were included in the analysis (Blomer 1986; Hooton 1989; Iravani 1991; Iravani 1995; Vogel 1984). Eight RCTs compared two different antibiotic regimens of at least five days duration (Bailey 1983; Fancourt 1984; Hill 1985; Little 1979; Martin 1983; McCarthy 1972; Pelta 1985; Zorbas 1995), two additional trials were excluded for they compared a single-dose antibiotic to ten-day (Schultz 1984) or three-day (Gellerman 1988) regimen. Another trial reported only clinical improvement but not cure (Ishihara 1998). One further study was excluded because it in-

cluded only elderly postmenopausal women (mean age 66 ±20) (Raz 1996). Two trials were excluded as they appeared to be quasi-randomised or criterion C in the Handbook (Charlton 1976; Fair 1980).

Thirty-two trials were included in the review (see *Table of included studies*). One trial compared two different antibiotics with subgroups of three-day and ten-day treatment regimens in each, and the results for these two drugs were regarded separately as two different trials (Gordin 1987a; Gordin 1987b).

The contact authors of these 32 included and two excluded as quasi-RCTs (Charlton 1976; Fair 1980) were contacted (by mail and if possible by e-mail) of whom 10 replied. Unpublished data were obtained for seven studies.

Patient characteristics

The included studies were performed between the years 1980-2002 and included 9605 randomised patients. The median number of patients/trial was 300.

In six trials (1356 patients) men were included (Basista 1991; Cox 1992; Hansen 1981; Menday 2000; Rapoport 1981; Stein 1987). Their number was less than 10% in each study group and it was impossible to separate the results for men and women for any of these trials. One additional trial (Bitsch 1985) included men, but analysis of men and women was separated and only data regarding women was used for this review.

Fourteen studies included women above 65 years of age (Basista 1991; Bitsch 1985; Cox 1992; Guibert 1997; Hansen 1981; Internordic 1988; Iravani 1999; Menday 2000; Piipo 1990; Rapoport 1981; Sandberg 1985; Stein 1987; Stein 1992; Tsugawa 1999). In all these 14 trials patients above 65 years made up the minority of the study groups and in 7 of these trials the mean age reported (33 to 45 years) was well below the upper limit we defined for this review (Basista 1991; Bitsch 1985; Guibert 1997; Hansen 1981; Rapoport 1981; Sandberg 1985; Stein 1992). Unfortunately, it was impossible to analyse data for patients below and above the age of 65 separately.

Nearly all trials defined bacteriuria as more than 10^5 CFU/ml for any bacteria or the same concentration for Gram-negative bacteria and 10^4 CFU/ml for *Staphylococcus*. Several studies included patients with lower urine bacteria concentration of 10^4 CFU/ml (Hovelius 1985; Neringer 1992; Stein 1992; Tsugawa 1999), 10^3 CFU/ml (Iravani 1999) and 10^2 CFU/ml (Hooton 1991) for any bacteria. In one trial, positive urine culture was not necessary for patient inclusion and the case definition was based on the clinical signs and pathologic urinalysis (Guibert 1997).

In two trials several women with asymptomatic bacteriuria were treated and taken into account for the bacterial cure results (Gordin 1987a; Gordin 1987b; Hooton 1991).

Antibiotic regimens

The same antibiotics in the three-day and 5-10 day groups were used in 19 trials, of these quinolones were used in six trials (Garcia 2002; Internordic 1988; Neringer 1992; Piipo 1990; Trienekens 1993; Tsugawa 1999), beta-lactams in eight (Gordin 1987b; Greenberg 1986; Hansen 1981; Hovelius 1985; Marsh 1980; Pitkajarvi 1990; Richards 1984; Sandberg 1985) and different combinations of sulfonamides and trimethoprim in five trials (Gordin 1987a; Gossius 1984; Gossius 1985; Iravani 1983; Trienekens 1989). In one of these studies different doses of the same antibiotic drug (pivmecillinam) were used in the two study groups (Hansen 1981).

Fourteen trials compared different antibiotics given in the three-day and in the 5-10 day groups. The drug in the three-day group was a quinolone in nearly all of these studies, and was compared to 5-10 day regimens of beta-lactam (Winwick 1981), different combinations of sulfonamides and trimethoprim (Basista 1991; Bitsch 1985; Butler 1983; Cox 1992; Hooton 1991; Stein 1987), another quinolone (Henry 1999; Guibert 1997; Stein 1992) or a combination of nitrofurantoin with trimethoprim-sulfamethoxazole (Iravani 1999). One additional trial compared three-day treatment with trimethoprim-sulfamethoxazole to seven-day treatment with any of a long list of antibiotics (Rapoport 1981). In two trials three-day therapy with beta-lactam was compared to seven-day treatment with another drug of the beta-lactam group (Menday 2000) or trimethoprim-sulfamethoxazole (Figueroa 1999).

METHODOLOGICAL QUALITY

Randomisation and allocation concealment

Adequate allocation concealment, using sealed envelopes or central randomisation, was described in 12 trials (Basista 1991; Bitsch 1985; Gordin 1987a; Gordin 1987b; Henry 1999; Hooton 1991; Hovelius 1985; Iravani 1999; Neringer 1992; Piipo 1990; Richards 1984; Sandberg 1985; Trienekens 1993). Allocation generation was adequate in all 12 and in additional six (Butler 1983; Gossius 1985; Marsh 1980; Pitkajarvi 1990; Stein 1987; Stein 1992). These studies used computer-generated lists or predetermined randomised codes. Randomisation methods were not described in all other trials.

Blinding

Ten trials were double-blinded (Henry 1999; Internordic 1988; Iravani 1999; Menday 2000; Neringer 1992; Piipo 1990; Stein 1992; Trienekens 1989; Trienekens 1993; Tsugawa 1999), one single-blinded (Richards 1984) and the remaining open RCTs.

ITT analysis

ITT analysis was presented in only two of the 32 trials included for treatment failure (Henry 1999; Iravani 1999). Dropouts and numbers of patients with positive urine cultures were reported by their allocation group in 21 of 32 trials presenting per protocol analysis for treatment failure, permitting a second ITT analysis

assuming dropouts as failures. The number of patients excluded from the analysis at the first follow-up ranged between 0-20% for bacteriological cure outcome and 0-26% for clinical (symptomatic) cure; at the second follow-up these numbers were 0-29% and 6-45%, respectively.

The first follow-up was performed between two to 15 days from the end of the treatment (short-term), and the second follow-up was performed four to 10 weeks from the treatment (long-term).

RESULTS

Trials were divided into two major subgroups: those with the same antibiotics in the two allocation groups and those with different drugs.

Effectiveness

Symptomatic failure

Short-term

Assessment of short-term symptomatic failure rate was possible in 24 trials (8752 patients). Data for efficacy analysis was available in 5165 patients. No significant difference between three-day and 5-10 day antibiotic treatment was observed (outcome 01: RR 1.06, 95% CI 0.0.88 to 1.28, P = 0.52), with no significant heterogeneity observed for this comparison (Chi^2 = 27.14, df = 23, P = 0.25, I^2 = 15.3%)

Separate analysis of trials with same or different antibiotic in the two treatment arms showed no significant difference. In 14 trials comparing the same antibiotic the RR was 1.15 (95% CI 0.95 to 1.39, outcome 01.01) in 10 trials with different antibiotics the RR was 0.90 (95% CI 0.62 to 1.29, outcome 01.02). No differences were shown after performing subgroup analyses for the factors: antibiotic classes (quinolones, beta-lactams, sulfonylamides with or without trimethoprim); allocation generation and concealment; or per cent of dropouts.

Long-term

Assessment of long-term symptomatic failure rate was available from eight trials (3141 patients). No difference was found between the two arms (outcome 03: RR 1.09, 95% CI 0.94 to 1.27). After performing subgroup analysis as for the first follow-up results no differences were shown.

A secondary ITT analysis counting dropouts as failures of treatment showed similar results (outcomes 02 and 04).

Bacteriologic failure

Short-term

Assessment of short-term bacteriological failure rate was possible in 31 trials (8874 patients). For efficacy analysis 5368 patients were included, the majority of the excluded persons having negative urine cultures after being allocated to one of the study regimens. Five to 10-day antibiotic regimen appeared to be superior to the three-day regimen although the result was not significant using the random effects model (outcome 05: RR 1.19, 95% CI 0.98 to 1.44, P = 0.08), but just significant with the fixed effect model (RR 1.20, 95% CI 1.00 to 1.44, P = 0.05). No significant heterogeneity was observed for this comparison (Chi^2 = 24.54, df = 29, P=0.70, I^2 = 0%). This advantage was observed in trials comparing the same antibiotic (outcome 05.01: RR 1.37, 95% CI 1.07 to 1.74; P = 0.01), and absent in the subgroup analysis of trials comparing different drugs (RR 0.96, 95% CI 00.68 to 1.35, P = 0.80). The trials using same antibiotic drug in the two treatment arms was further divided for subgroup analysis based on the different antibiotic classes (outcome 06) and showed that the results were not significantly influenced by the drug choice. The results remain unchanged after performing the other subgroup analyses (for allocation generation and concealment class, trial size or per cent of dropouts).

A secondary ITT analysis for the short-term results was only possible in 21/31 trials. Its results showed actually no difference between the two treatment regimens, (outcome 07: RR 0.92, 95% CI 0.80 to 1.06). No difference was observed in any of the subgroups analyses.

Long-term

Assessment of the long-term bacteriological failure rate was possible in 18 trials (3715 patients) (13 trials and 2502 patients in the same antibiotic subgroup; five trials and 1213 patients in the different regimens subgroup). The 5-10-day antibiotic regimen was superior to the three-day regimen (outcome 08: RR 1.31, 95% CI 1.08 to 1.60, P = 0.006) and no significant heterogeneity was observed (Chi^2 = 24.40, df = 17, P = 0.11, I^2 = 30.3%). A significant difference was shown in the subgroup of trials with the same drug in both allocation arms (outcome 08.01: RR 1.43, 95% CI 1.19 to 1.73, P = 0.0002), while no difference was observed between 5-10 day and three day regimens when different drugs were used. These results also remain unchanged after performing the additional subgroup analyses for antibiotic class (outcome 09), allocation generation, trial size and concealment class or per cent of dropouts.

A secondary ITT analysis for the second follow-up results showed the same results as the efficacy analysis, confirming the observed significant advantage of 5-10 day antibiotic regimen over the three-day regimen for all trials (outcome 10: RR 1.19, 95% CI 1.06 to 1.35, P = 0.004), and for the subgroup of the same drug regimen (outcome 10.01: RR 1.26, 95% CI 1.08 to 1.47, P = 0.003). The results of the subgroup analysis for the class of antibiotic drug are shown in outcome 11.

Pyelonephritis

Only five of the included trials reported the incidence of pyelonephritis (Cox 1992; Gossius 1984; Gossius 1985; Hovelius 1985; Winwick 1981). Only two cases of pyelonephritis were reported, both in the three-days therapy groups (Gossius 1984; Gossius 1985). As this outcome was extremely uncommon in the population of young women with uncomplicated lower UTI, no dif-

ference could be observed between the two treatment regimens (outcome 13).

Adverse effects

All side effects were observed more frequently in the 5-10 day regimen than in the three-day group. The risk for the development of any side effect during therapy was 17% lower in the three-day group (outcome 12: RR 0.83, 95% CI 0.74 to 0.93, P = 0.0010). This difference was more prominent in trials comparing the same antibiotic (outcome 12.01: RR 0.76, 95% CI 0.63 to 0.92) and especially when the drug was sulfonylamide/trimethoprim (outcome 20: RR 0.40, 95% CI 0.19 to 0.88).

A substantially lower percentage of patients had to discontinue therapy in the three-day group, (outcome 14: RR 0.51, 95% CI 0.328 to 0.91, P = 0.02), particularly when the same drug was given in the two groups (outcome 14.01: RR 0.35, 95% CI 0.12 to 0.98, P = 0.04).

Gastrointestinal side effects appeared less frequently during three-day treatment (outcome 15: RR 0.81, 95% CI 0.67 to 0.94, P = 0.02). The difference in the frequency of development a skin rash was significant in the trials comparing the same antibiotic (outcome 16.01: RR 0.51,95% CI 0.33 to 0.77, P = 0.002), while no such difference was observed in the trials with different drugs (outcome 16.02: RR 0.69, 95% CI 0.21 to 2.28). The rate of side effects related to central nervous system was also slightly more frequent in the 5-10 day group, but this difference was not significant overall (outcome 17: RR 0.83, 95% CI 0.65 to 1.06, P = 0.13).

As for anaphylactic reactions, only two trials described one case, both in the 5-10 day group (Butler 1983; Gossius 1984), and no difference could be observed between the two treatment regimens.

Resistant organisms

Only a minority of the included trials described the antibiotic resistance profile of the bacteria cultured from patients urine before and after treatment. In two studies using quinolones in both treatment arms, no persistent or recurrent pathogen developed resistance to the study drugs during treatment or during the follow-up period (Internordic 1988; Neringer 1992). In one trial studying thee-day versus seven-day pivmecillinam regimens (Richards 1984) the number of resistant bacteria isolates after therapy did not change, and an additional trial using the same drug (Hansen 1981) showed only total rate of resistance development after therapy without specification to different study groups. Two studies using sulfonamide (Iravani 1983) and co-trimoxazole (Trienekens 1989) mentioned the prevalence of the drug-resistant *E. coli* in the failure cases, but it was unclear whether these were primary resistant strains or the resistance developed during the treatment. One study (Basista 1991) showed significant difference in the development of urine bacteria resistance between the three-day (no cases) and the seven-day (three cases) protocols but the drugs used in the two treatment arms were different (quinolone versus trimethoprim/sulfamethoxazole), so this data is of only limited value.

Dropouts and selection bias

Funnel plots for symptomatic (Figure 01 - *Funnel plot symptomatic failure*) and bacteriological failure (Figure 02 - *Funnel plot bacteriologic failure*) showed that several smaller studies favouring the three-day regimen may be missing from this review. It is important to mention that all the studies included in this meta-analysis were planned to check the hypothesis that the three-day antibiotic therapy is as effective as a longer one.

The number of patients excluded from each study arm was nearly equal, both for symptomatic and bacteriological outcomes assessment.

DISCUSSION

Thirty-two RCTs, including 9605 patients, comparing three-day antibiotic treatment to 5-10 day treatment for the empirical therapy of uncomplicated UTIs in the young and middle-aged women were analysed. Two outcomes were chosen for comparison: symptomatic failure and bacteriological failure as defined by positive post-treatment urine cultures. Primary treatment failures and recurrences or re-infections were considered together as therapy failures, for in the majority of the studies no distinction could be made between them.

Symptomatic failure rates did not differ significantly both in the short-term (RR 1.06, 95% CI 0.88 to 1.28) or long-term (RR 1.07, 95% CI 0.99 to 1.16) after treatment with three-day or 5-10 day regimens. No information about the timing of the symptomatic cure could be found in the included studies.

Five to 10 day antibiotic regimen was more effective than three day therapy, keeping the patients' urine sterile two to 15 days after the end of treatment (same drug therapy RR 1.37, 95% CI 1.07 to 1.74, P = 0.01). This means that 41 women would have to be treated for seven days to prevent one case of recurrence or persistence of bacteriuria for a short period. The ITT analysis showed no difference between short and long treatment regimens. Data considering the numbers of randomised patients with positive urine cultures were unattainable from the published articles or any additional source in six major studies in this subgroup (Garcia 2002; Gossius 1984; Gossius 1985; Marsh 1980; Richards 1984; Trienekens 1993), so it was impossible to include these trials into the ITT analysis. This fact, together with the high rate of dropouts, could explain why we failed to show a significant effect of therapy duration on the short-term bacteriologic failure rates in the ITT analysis.

A larger advantage of 5-10 day over three-day antibiotic therapy in preventing bacteriological failure was observed after 4-10 weeks (RR 1.43, 95% CI 1.19 to 1.73, P = 0.0002) when treatment with the same drug was compared (number needed to treat (NNT) = 4). This difference remained significant also with an ITT analysis (RR 1.26, 95% CI 1.08 to 1.47, P = 0.003). It is important to mention

that the advantage of the longer therapy in terms of bacteriological success appeared to be independent of the antibiotic class chosen for UTI treatment including quinolones.

One reason for the advantage of longer therapy might be the survival of bacteria in subepithelial loci of the lower urinary tract after a shorter course of antibiotic treatment. Recently the ability of *E. coli* to invade epithelial cells and create biofilms with pod-like bulges on the bladder surface was discovered (Anderson 2003). These pods contain bacteria encased in a polysaccharide-rich matrix surrounded by a protective shell of uroplakin, and allow bladder infections to persist in the face of robust host defences and short-term antibiotic treatment. Another recently published study showed that asymptomatic bacteriuria is associated with an increased risk of symptomatic UTI in young women (Hooton 2000). Thus, bacteriological failure might also carry a clinical significance for the patients.

The probable cause for the absence of such difference in the trials comparing different drugs in the two study groups was the fact that all but three of these trials compared three-day quinolone therapy with 5-10 day regimen of beta-lactams or sulfonylamides/ trimethoprim. Both the higher urine concentration and the lower rate of bacteria drug resistance favoured the newer quinolones. When trying to answer the question concerning the optimal treatment duration for UTI one should probably consider trials comparing the same drug in the two therapy groups.

We found a discrepancy between symptomatic cure, which was not influenced by treatment duration, and bacteriological cure. Fewer included trials showed results of symptomatic cure as compared to bacteriologic results (21 versus 31 studies at the first follow-up and 10 versus 18 at the second follow-up, respectively). This could be one of the reasons explaining the discrepancy between the efficacy results for these two outcomes.

Not surprisingly, the cost of the higher bacteriological cure rates after longer antibiotic therapy is a significantly higher rate of adverse events, including those leading to treatment discontinuation. Again, the difference was observed in the trials dealing with two regimens of the same drug. The per cent of patients who stopped the treatment because of adverse effects in the three-day group was 1.5% compared to 3.2% in the 5-10 day group (RR 0.35, 95% CI 0.12 to 0.98, P = 0.04), number needed to harm = 79. However all adverse effects were minor.

We performed sensitivity analyses that did not detect sources of bias originating in studies'design, methodology or class of antibiotic drug used. However, allocation concealment was known to be adequate in only 12 of included 31 trials, and only 11 were blinded. All but two of the included studies did not adhere to the principle of ITT analysis. Larger numbers of patients excluded from the efficacy analysis was due to negative urine cultures after admission, which should be considered as exclusions rather than dropouts, but the high rate of dropouts during the follow-up was a major problem in many included studies.

AUTHORS' CONCLUSIONS

Implications for practice

The present practice of treating uncomplicated UTIs in young women for only three days to achieve symptomatic relief is probably sufficient for the majority of patients. However it leaves a significant risk of recurrent or persistent bacteriuria independent of the class of the drug.

Pending further research, antibiotic treatment for 5-10 days could be considered for women in whom bacteriological eradication might be of importance: e.g. women suffering from recurrent and painful lower UTIs, planning pregnancy or with underlying disorders. Ultimately the decision regarding therapy duration should be taken with the patient, balancing the higher bacteriological cure rate versus the similar symptomatic outcome and increased risk for adverse events.

The risk of pyelonephritis development as a function of therapy duration is probably irrelevant as it is an extremely rare event in patients with lower UTI.

Implications for research

We propose that future research in this area should address the question of the link between the bacteriuria and symptomatic UTIs. Future trials should use the same antibiotic drug in the different treatment duration groups to exclude the effect of antibiotic efficacy. It is important to perform antibiotic susceptibility tests during the follow-up to assess whether duration of the antibiotic therapy influences the rate of resistance development.

The duration of treatment in special groups of women (i.e. those suffering from recurrent and painful lower UTIs, planning pregnancy, or with underlying disorders) should be addressed in further studies.

POTENTIAL CONFLICT OF INTEREST

None known.

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** Indicates the major publication for the study*

TABLES

Characteristics of included studies

Study	Basista 1991
Methods	Randomisation: computer-generated Blinding: none Intention-to-treat: no information Interim analysis: no information Excluded for efficacy analysis: 40/97 patients (19+21) - 25 of them (14+11) due to negative urine cultures Excluded for safety analysis: 3/97 (2+1) Follow-up: 4 to 10 days after treatment
Participants	USA (8 centers) 97 patients (over 90% - female and white) Age: 18-84 (mean = 33) Data collection: no information

Characteristics of included studies (*Continued*)

	Bacteriuria > 10^5 CFU/ml
Interventions	ofloxacin 200 mg x 1 for 3 days vs TMP-SMX 160/800 mg x 2 for 7 days
Outcomes	Clinical cure (but results not shown) Bacteriological cure Adverse effects
Notes	90% - female and white (the exact number of males not mentioned) Age: 18-84 The trial was terminated early by the sponsor's medical monitor after 97 patients (instead of 150) involved Different antibiotics were compared
Allocation concealment	A – Adequate

Study	**Bitsch 1985**
Methods	Randomisation: sealed envelopes method Blinding: no information Intention-to-treat: no information Interim analysis: no information Excluded: 84/394 (30 - no urine cultures was taken; 41 - no significant bacteriuria; 13 - dropouts) Follow-up : 2 days and 10 weeks after end of treatment
Participants	Denmark 394 patients (92% - non-pregnant women) Age: 16-70 (mean = 38) Data collection: 5/81 - 5/82 Bacteriuria > 10^5 CFU/ml
Interventions	pivmecillinam 400 mg x 3 for 3 days vs sulfametizol 1 g x 2 for 6 days
Outcomes	Clinical cure Bacteriological cure Adverse effects
Notes	~8% (25 of 310 included in efficacy analysis) were males but results for women with uncomplicated lower UTI only can be separated Different antibiotics were compared
Allocation concealment	A – Adequate

Study	**Butler 1983**
Methods	Randomisation: randomised list Blinding: no information Intention-to-treat: no information Interim analysis: no information Excluded for clinical efficacy: 16/141 (12 - lost to follow-up; 3 - stopped treatment due to side effects; 1 - admitted to hospital due to gastritis) Excluded for bacteriological efficacy analysis: 75/141 (no significant bacteriuria) Follow-up: 2-3 days after end of treatment and 4 week after it
Participants	UK 110 non-pregnant women Age: 18-32 (median=20)

Characteristics of included studies (*Continued*)

	Data collection: no information Bacteriuria > 10^5 CFU/ml
Interventions	nalidixic acid 660 mg + sodium citrate 3.75 g x 3 for 3 days vs TMP/SMX 160/800 mg x 2 for 5 days
Outcomes	Clinical cure Bacteriological cure
Notes	Different antibiotics were compared
Allocation concealment	B – Unclear

Study	**Cox 1992**
Methods	Randomisation: no information Blinding: no information Intention-to-treat: no information Interim analysis: no information Excluded for efficacy analysis: 65/202 (39 - diagnosis not confirmed; 9 - resistance or intermediate sensitivity in TMP/SMX group; 7 - no compliance to treatment; 6 - lost to follow-up; 4 - reasons not reported) Excluded for safety analysis: 2/202 patients Follow-up: 5-9 days after treatment
Participants	USA 202 patients Males: 3 of 137 finally analysed Age: 18-80 (female) 37-46 (male) Data collection: 2/88 - 10/88 Bacteriuria > 10^5 CFU/ml
Interventions	ofloxacin 200 mg x 1 for 3 days vs TMP/SMX 160/800 mg x 2 for 7 days
Outcomes	Clinical cure Bacteriological cure Adverse effects
Notes	Males not excluded Age of females: 18-80 Different antibiotics were compared
Allocation concealment	B – Unclear

Study	**Figueroa 1999**
Methods	Randomisation: no information Blinding: No Intention-to-treat: no information Interim analysis: no information Follow-up: 7-10 days and 21-28 days after treatment
Participants	Mexico 60 non-pregnant women Age: 18 - 50 Bacteriuria > 10^5 CFU/ml Data collection: no information
Interventions	ceftibuten 400 mg single dose vs

	ceftibuten 400 mg x 1 for 3 days vs TPM/SMX 160/800 mg x 2 for 7 days
Outcomes	Clinical cure Bacteriological cure Adverse effects
Notes	Different antibiotics were compared Additional group of patients was studied - a single-dose of ceftibuten Only short-term results shown
Allocation concealment	B – Unclear

Study	**Garcia 2002**
Methods	Randomisation: no information Blinding: no information Intention-to-treat: no information Interim analysis: no information Excluded for efficacy analysis: 33/151 (5 - bacteria resistant to norfloxacin; 12 - negative cultures; 16 - lost for follow-up) Follow-up: 3 days and 30 days after treatment
Participants	Spain 151 non-pregnant women Age: above 18 Data collection: 1998 - 1999 Bacteriuria > 10^5 CFU/ml
Interventions	norfloxacin 400 mg x 2 for 3 days vs norfloxacin 400 mg x 2 for 7 days
Outcomes	Clinical cure Bacteriological cure
Notes	Upper age limit not mentioned Only short-term results shown
Allocation concealment	B – Unclear

Study	**Gordin 1987a**
Methods	Randomisation: latin square method Blinding: No Intention-to-treat: no information Interim analysis: no information Excluded to efficacy analysis: 27/159 (20- negative urine cultures; 4- lost to follow-up; 3- discontinued treatment due to side effects) Follow-up : 3-5 days and 4 weeks after treatment
Participants	Finland 159 women Age : 17-63 (mean = 32) Data collection : 9/82 - 10/84 Bacteriuria > 10^5 CFU/ml
Interventions	TMP-sulfadiazine(160mg+500mg) x 2 for 3 days vs TMP-sulfadiazine(160mg+500mg) x 2 for 10 days

Characteristics of included studies (*Continued*)

Outcomes	Bacteriological cure Adverse effects
Notes	7 of 159 - patients with asymptomatic bacteriuria included A trial with 4 groups was analysed as two separate subtrials
Allocation concealment	A – Adequate

Study	**Gordin 1987b**
Methods	Randomisation: latin square method Blinding: No Intention-to-treat: no information Interim analysis: no information Excluded to efficacy analysis: 27/159 (20- negative urine cultures; 4- lost to follow-up; 3- discontinued treatment due to side effects) Follow-up: 3-5 days and 4 weeks after treatment
Participants	Finland 159 women Age: 17-63 (mean = 32) Data collection : 9/82 - 10/84 Bacteriuria > 10^5 CFU/ml
Interventions	pivmecillinam 200mg x 3 for 3 days vs pivmecillinam 200mg x 3 for 10 days
Outcomes	Bacteriological cure Adverse effects
Notes	7 of 159 - patients with asymptomatic bacteriuria included A trial with 4 groups was analysed as two separate subtrials
Allocation concealment	A – Adequate

Study	**Gossius 1984**
Methods	Randomisation: no information Blinding: no information Intention-to-treat: no information Interim analysis: no information Excluded - 185/464 (143 - negative cultures; 7 - resistant organisms; 11 - lost to follow up; 24 - adverse reactions necessitated cessation of treatment) (Side effects assessed in 408 patients) Follow-up period: 2 weeks and 6 weeks after treatment
Participants	Norway 464 women Age: 16-60 Data collection: no information Bacteriuria > 10^5 CFU/ml
Interventions	TMP-SMX (160mg+800mg) x 2 for 3 days vs TMP-SMX(160mg+800mg) x 2 for 10 days
Outcomes	Clinical cure Bacteriological cure Adverse effects

Characteristics of included studies (*Continued*)

Notes	Additional group of patients was studied - a single-dose TMP-SMX
Allocation concealment	B – Unclear

Study	**Gossius 1985**
Methods	Randomisation: boxes with code numbers and tablets wrapped in plain alluminium foil Blinding: no information Intention-to-treat: no information Interim analysis: no information Excluded: 63/135 (44 - nonsignificant pre-therapy bacteriuria; 6 - lost to follow up; 2 - initially resistant organisms; 1 - developed pyelonephritis(in 3-day group); 7 - side effects leading to therapy cessation) Follow-up: 2 and 6 weeks after treatment
Participants	Norway 135 women Age: 16 to 60 Data collection: no information Bacteriuria > 10^5 CFU/ml
Interventions	TMP 200 mg x 2 for 3 days vs TMP 200 mg x 2 for 10 days
Outcomes	Clinical cure Bacteriological cure Adverse effects (for 114 patients who completed treatment)
Notes	Clinical response for patients without significant bacteriuria mentioned for total number (not devided for the treatment groups)
Allocation concealment	B – Unclear

Study	**Greenberg 1986**
Methods	Randomisation: no information Blinding: no information Intention-to-treat: no information Interim analysis: no information Excluded: 15/126 at 3-days follow-up visit ; 49/126 at 2-weeks follow-up visit Follow-up: 3 days, 2 weeks and 4 weeks post-therapy
Participants	USA 126 non-pregnant women Age: > 12 Data collection: 4/83 - 11/84 Bacteriuria > 10^5 CFU/ml
Interventions	cefadroxil 1 g single dose vs cefadroxil 500 mg x 2 for 3 days vs cefadroxil 500 mg x 2 for 7 days vs TMP/SMX 320/1600 mg single dose vs TMP/SMX 160/800 mg x 2 for 3 days
Outcomes	Clinical cure Bacteriological cure

Characteristics of included studies (*Continued*)

	Adverse effects
Notes	Different antibiotics were compared Two additional groups of single dose treatment Only two groups (cefadroxil 500 mg x 2 for 3 vs 7 days) will be analysed here
Allocation concealment	B – Unclear

Study	**Guibert 1997**
Methods	Randomisation: no information Blinding: no information Intention-to-treat: yes Interim analysis: no information Follow-up: 14 days after end of treatment Excluded to clinical efficacy analysis: 81/421 (non-compliance to study protocol)
Participants	France 421 non-pregnant women Data collection : 12/94 - 6/95 Bacteriuria: not defined (case definition by clinical signs and symptoms)
Interventions	lomefloxacin 400 mg x 1 for 3 days vs norfloxacin 400 mg x 2 for 10 days
Outcomes	Clinical cure Adverse effects
Notes	Different antibiotics were compared Bacteriuria: not defined
Allocation concealment	B – Unclear

Study	**Hansen 1981**
Methods	Randomisation: no information Blinding: no information Intention-to-treat: no information Interim analysis: no information Follow-up: 2 days and 8-10 weeks after end of treatment
Participants	Denmark 221 patients Women - 92% (non-pregnant) Age: 16-80 (mean = 39) Data collection: no information Bacteriuria > 10^5 CFU/ml
Interventions	pivmecillinam 400 mg x 3 for 3 days vs pivmecillinam 200 mg x 3 for 7 days
Outcomes	Bacteriological cure Adverse effects
Notes	8% - males Different antibiotic doses were compared Multicenter trial
Allocation concealment	B – Unclear

Characteristics of included studies (*Continued*)

Study	**Henry 1999**
Methods	Randomisation: allocation numbers generated by the pharmaceutic company; cards with the listing of the medication distributed to the centers Blinding: double-blinded, double-dummy Intention-to-treat: Yes Interim analysis : no information Excluded to clinical efficacy analysis: 221/1175 Excluded to bacteriological efficacy analysis: 685/1175 Follow-up: 13 to 15 days after beginning of the treatment and 4 to 6 weeks after therapy
Participants	USA 1175 non-pregnant women Age: 18-64 (mean=34) Data collection: 1/94 - 2/95 Bacteriuria > 10^5 CFU/ml
Interventions	sparfloxacin 400 mg single dose vs sparfloxacin 400 mg on the first day followed by 200 mg x 1 (3 days total) vs ciprofloxacin 250 mg x 2 for 7 days
Outcomes	Clinical cure Bacteriological cure Adverse effects
Notes	Multicenter trial Additional group of single-dose drug Higher percentage of patients with previous urinary tract surgery in the 7-day group More drop-out in the 7-day group than in 2 other groups Different antibiotics were compared
Allocation concealment	A – Adequate

Study	**Hooton 1991**
Methods	Randomisation: computer-generated randomization list provided by pharmaceutical company, patients allocated sequentially Blinding: none Intention-to-treat: no information Interim analysis: no information Excluded to efficacy analysis: 6/150 (5 - no significant bacteriuria; 1 - no follow-up) Follow-up: 5-9 days and 4-6 weeks after treatment
Participants	USA 150 non-pregnant women Age: >18 (mean=24-25) Data collection : no information Bacteriuria > 10^2 CFU/ml with symptoms or Bacteriuria > 10^5 CFU/ml asymptomatic
Interventions	ofloxacin 400 mg single dose vs ofloxacin 200 mg x 1 for 3 days vs TMP/SMX 160/800 mg x 2 for 7 days
Outcomes	Bacteriological cure Adverse effects

Characteristics of included studies (*Continued*)

Notes	Significant bacteriuria defined as > 10^2 CFU/ml + symptoms or pyuria Asymptomatic bacteriuria treated Different antibiotics were compared Additional single dose group
Allocation concealment	A – Adequate

Study	**Hovelius 1985**
Methods	Randomisation: sealed envelopes with treatment protocol Blinding: No Intention-to-treat: no information Interim analysis: no information Excluded: 38/160 - No significant bacteriuria Follow-up: 1 week and 4 weeks after treatment
Participants	Sweden 160 women Age: 15-45 Data collection: no information Bacteriuria > 10^4 CFU/ml
Interventions	pivmecillinam 400 mg x 3 for 3 days vs pivmecillinam 200 mg x 3 for 7 days (and nalidixic acid 1 g x 3 for 3 vs 7 days)
Outcomes	Bacteriological cure Adverse effects
Notes	1) Only pivmecillinam groups can be analysed due to treatment regimen change in patients of nalidixic acid groups 2) Different doses of pivmecillinam were used 3) 2 patients with S.saprophyticus <10^4 CFU included separately 4) Age: 15-45
Allocation concealment	B – Unclear

Study	**Internordic 1988**
Methods	Randomisation: no information Blinding: double-blinded Intention-to-treat: no information Interim analysis: no information Excluded for safety analysis: 6/485 patients Excluded for efficacy analysis: 112/485 (84 - no significant bacteriuria; 3 - lost to follow-up; 8 - treatment less than 13 doses; 17 - others) Follow-up: “short-term” - 3 to 13 days after treatment and “accumulated efficacy” - worst result 3 until 45 days after treatment
Participants	Norway, Sweden 485 non-pregnant women Age: 18-80 Data collection: 11/85 - 6/87 Bacteriuria > 10^5 CFU/ml for Gram-negative and 10^4 for Staphylococcus saprophyticus
Interventions	norfloxacin 400 mg x 2 for 3 days vs norfloxacin 400 mg x 2 for 7 days

Characteristics of included studies (*Continued*)

Outcomes	Clinical cure Bacteriological cure Adverse effects
Notes	Age: 18-80 Multicenter trial
Allocation concealment	B – Unclear

Study	**Iravani 1983**
Methods	Randomisation: no information Blinding: no information Intention-to-treat: no information Interim analysis: no information Excluded: 12/158 (reasons not mentioned) Follow-up: 1, 2 and 4 weeks after treatment
Participants	USA 158 women college students Data collection: no information Bacteriuria > 10^5 CFU/ml
Interventions	sulfisoxazole 2 g as first dose followed by sulfisoxazole 1 g x 4 for 3 days vs sulfisoxazole 1g x 4 for 7 days vs sulfisoxazole 1 g x 4 for 14 days vs sulfisoxazole 1 g x 4 for 21 days
Outcomes	Clinical cure Bacteriological cure
Notes	30 patients had costovertebral tenderness on examination Age not mentioned (“college coeds”) Groups of 7, 14 and 21 days will be analysed together (“multi-days”)
Allocation concealment	B – Unclear

Study	**Iravani 1999**
Methods	Randomisation: opaque gelatin capsules with medication or placebo Blinding: double blinded Intention-to-treat: yes Interim analysis: no information Excluded: 192/713 (128 - negative cultures; 28 - cultures not obtained; 14 - entry criteria violations; 12 - inadequate duration of treatment; 3 - insufficient pretreatment colony counts; 3 - administration of concominant antibiotics; 2 - noncompliance; 1 - no follow-up; 1 - resistant organism) Follow-up: 4-10 days and 4-6 weeks after treatment
Participants	USA 713 women Age: 18-85 Data collection : no information Bacteriuria > 10^3 CFU/ml
Interventions	ciprofloxacin 100 mg x 2 for 3 days vs

Characteristics of included studies (*Continued*)

	TMP-SMX 160/800 mg x 2 or nitrofurantoin 100 mg x 2 for 7 days
Outcomes	Clinical cure Bacteriological cure Adverse effects
Notes	Different antibiotics were compared Multicenter trial Age: 18-85 Bacteriuria > 10^3 CFU/ml Two groups of 7-days treatment will be analysed together
Allocation concealment	A – Adequate

Study	**Marsh 1980**
Methods	Randomisation: randomised list Blinding: no information Intention-to-treat: no information Interim analysis: no information Excluded for clinical efficacy: 16/141 (12 - lost to follow-up; 3 - stopped treatment due to side effects; 1 - admitted to hospital due to gastritis) Excluded for bacteriological efficacy analysis: 75/141 (no significant bacteriuria) Follow-up: 2-3 days after end of treatment and 4 week after it
Participants	UK 141 non-pregnant women Age: 15-55 Data collection: no information Bacteriuria > 10^5 CFU/ml
Interventions	pivmecillinam (dose not mentioned) for 3 days vs pivmecillinam (dose not mentioned) for 7 days
Outcomes	Clinical cure Bacteriological cure Adverse effects
Notes	Results of clinical cure are presented in the form of symptom score (mean and range) - cannot be analysed here Doses of antibiotics not mentioned
Allocation concealment	B – Unclear

Study	**Menday 2000**
Methods	Randomisation: no information Blinding: double-blind (double-dummy technique) Excluded for efficacy analysis: 224/440 (129 - <10^5 CFU/ml of bacterial pathogen; 37 - inadequate urinary cultures; 54 - bacteria in vitro susceptibility not confirmed; 3 - non-compliance or concominant antibiotic use; 2 - violated protocol inclusion criteria) Follow-up: day 10 (+/-2) and day 14 (+/-2) from the beginning of treatment
Participants	UK 440 patients Women: 212 of 216 patients included in efficacy analysis Age: 18-87 years Bacteriuria > 10^5 CFU/ml

Characteristics of included studies (*Continued*)

Interventions	pivmecillinam 200 mg x 3 for 3 days vs cephalexin 250 mg x 4 for 7 days
Outcomes	Clinical cure Bacteriological cure Adverse effects
Notes	Different antibiotics doses were compared Age: 18-87 years 4 of 216 patients included in efficacy analysis were men Results of clinical cure and improvement are presented together (it's impossible to separate between them)
Allocation concealment	B – Unclear

Study	**Neringer 1992**
Methods	Randomisation: computer-generated randomisation schedule Blinding: double-dummy method Intention-to-treat: no information Interim analysis: no information Excluded for efficacy analysis: 116/703 (no significant bacteriuria) Follow-up : 5-9 days posttreatment and "accumulated results" at 3-4 weeks posttreatment
Participants	Sweden 703 non-pregnant women Age : 18-65 Data collection : 8/88 - 1/90 Bacteriuria > 10^4 CFU/ml
Interventions	lomefloxacin 400 mg x 1 for 3 days vs lomefloxacin 400 mg x 1 for 7 days vs norfloxacin 400 mg x 2 for 7 days
Outcomes	Clinical cure Bacteriological cure Adverse effects
Notes	One additional group of another antibiotic was included as a 7-day treatment (norfloxacin) Only two groups (lomefloxacin 400 mg x 1 for 3 vs 7 days) will be analysed here
Allocation concealment	A – Adequate

Study	**Piipo 1990**
Methods	Randomisation: no information Blinding: double-blind Intention-to-treat: no information Interim analysis: no information Excluded for efficacy analysis: 73/400 (60 - no significant bacteriuria; 4 - no posttreatment cultures; 4 - change to other antibiotics; 4 - patients did not take drugs as prescribed; 1 - lost for follow-up) Follow-up: 3 to 13 days posttreatment and accumulated efficacy (worst result 3 days posttreatment to day 45 after treatment start)
Participants	Finland 400 non-pregnant women Age: 18-80 Data collection : no information

Characteristics of included studies (*Continued*)

	Bacteriuria > 10^5 CFU/ml (10^4 for Staphylococcus saprophyticus)
Interventions	norfloxacin 400 mg x 2 for 3 days vs norfloxacin 400 mg x 2 for 7 days
Outcomes	Clinical cure Bacteriological cure Adverse effects
Notes	Age: 18-80 (results for accumulated long-term efficacy showed for women 18 to 65 years old separately)
Allocation concealment	A – Adequate

Study	**Pitkajarvi 1990**
Methods	Randomisation: envelope method Blinding: no information Intention-to-treat: yes Interim analysis: none Excluded for clinical and bacteriologicl effect: 46/345 (no growth in th urine cultures) - 23 in both groups Follow-up: 5 days and 4-5 weeks after treatment
Participants	Finland 345 women Age: 16-65 (mean=35) Data collection: no information Bacteriuria > 10^5 CFU/ml (10^4 for Staphylococcus saprophyticus)
Interventions	pivmecillinam 400 mg x 3 for 3 days vs pivmecillinam 200 mg x 3 for 7 days
Outcomes	Clinical cure Bacteriological cure Adverse effects
Notes	Different antibiotics doses were compared
Allocation concealment	B – Unclear

Study	**Rapoport 1981**
Methods	Randomisation: no information Blinding: no information Intention-to-treat: no information Interim analysis: none Excluded: all the cases without significant bacteriuria; 16 of 91 with bacteriuria (lost at follow-up) Follow-up: 10 to 14 days after treatment
Participants	UK 187 patients Women: 69 of 75 included in analysis Mean age: 45(14-78) Data collection: 3/79 - 10/79 Bacteriuria > 10^5 CFU/ml
Interventions	TMP-SMX 2 tabs x 1 for 3 days vs different drugs* for 7 days

Characteristics of included studies (*Continued*)

	(* TMP-SMX - 17, sulfamethizole - 4, sulfadimidine - 4, amoxicillin - 6, mecillinam - 2, nalidixic acid - 2, nitrofurantoin -2)
Outcomes	Clinical cure Bacteriological cure
Notes	Age: 14-78 years Different antibiotics were compared No outcomes in subgroups of antibiotics in the 7-days group 6 of 75 included in the analysis are males
Allocation concealment	B – Unclear

Study	**Richards 1984**
Methods	Randomisation: numbered sealed envelopes (opaque not mentioned) Blinding: Single blinded (investigator) Intention-to-treat: no information Interim analysis: no information Excluded - 8 of 183 (3 - not completed the course due to side effects; 3 - lost to follow-up; 1 - age > 55; 1 - change in treatment due to worsening symptoms) Follow-up: 1 week after treatment
Participants	UK 183 non-pregnant women Age: 17-55 Data collection: no information Bacteriuria > 10^5 CFU/ml
Interventions	pivmecillinam 400 mg x 2 for 3 days vs pivmecillinam 400 mg x 2 for 7 days
Outcomes	Clinical cure Bacteriological cure Adverse effects
Notes	Multicentre study
Allocation concealment	A – Adequate

Study	**Sandberg 1985**
Methods	Randomisation: randomisation tables, sealed opaque envelopes containing the allocation number Blinding: none (open) Intention-to-treat: no information Interim analysis: yes (Henning 1982) Excluded : 80/310 (39 - non-significant bacteriuria; 11 - unknown urine test results; 10 - resistant bacteria; 13 - sensitivity testing for antibiotic not performed; 4 - lost to follow-up; 1 - male; 2 - known anomalies of urinary tract) Follow-up: 1 week and 5 weeks after the end of treatment
Participants	Sweden 310 non-pregnant women Age: 16-76 (mean = 35.7) Data collection : 9/81 - 12/82 Bacteriuria > 10^5 CFU/ml (10^4 for Staphylococcus saprophyticus)
Interventions	cefadroxil 1 g x 1 for 3 days vs cefadroxil 1 g x 1 for 7 days

	vs amoxycillin 375 mg x 3 for 7 days
Outcomes	Both clinical and bacteriological cure Adverse effects
Notes	Different antibiotics were compared Two groups of 7-days treatment with different antibiotics were compared with one 3-days group Only two groups (cefadroxil 1 g x 1 for 3 vs 7 days) will be analysed here Interim analysis= Henning1982
Allocation concealment	A – Adequate

Study	**Stein 1987**
Methods	Randomisation: a preassigned random - number code Blinding: none Intention-to-treat: yes Interim analysis: no information Excluded for efficacy analysis: No significant bacteriuria; Not available for follow-up Follow-up: 5 to 9 days , 4 to 6 weeks
Participants	USA 209 patients (192 of 209 - women) Age: 17-85 Data collection: no information Bacteriuria > 10^5 CFU/ml
Interventions	norfloxacin 400 mg x 2 for 3 days vs TMP-SMX 160/800 mg x 2 for 10 days
Outcomes	Clinical cure Bacteriological cure Adverse effects
Notes	Age: 17-85 Different antibiotics were compared 17 of 209 patients - males
Allocation concealment	B – Unclear

Study	**Stein 1992**
Methods	Randomisation: a preassigned random - number code Blinding: double-blind Intention-to-treat: no information Interim analysis: no information Excluded for efficacy evaluation: 184/404 (most common reason - lack of pretherapy urinary pathogen) No drop-outs to safety analysis Follow-up: 5 to 9 days after completion of therapy
Participants	USA 404 non-pregnant women Age : > 18 mean = 44 ; 81/404 - age 65 or more Data collection: no information Bacteriuria > 10^4 CFU/ml
Interventions	temafloxacin 400 mg x 1 for 3 days vs

Characteristics of included studies (*Continued*)

	ciprofloxacin 250 x 2 for 7 days
Outcomes	Clinical cure Bacteriological cure Adverse effects
Notes	81/404 - age 65 or more Different antibiotics were compared
Allocation concealment	B – Unclear

Study	**Trienekens 1989**
Methods	Randomisation: no information Blinding: double dummy technique, placebo tablets identical to active drug Intention-to-treat: no information Interim analysis: no information Follow-up: 1, 2 and 6 weeks after entry
Participants	The Netherlands 327 non-pregnant women Age: 12-65 Data collection : 1/88 - 4/89 Bacteriuria > 10^5 CFU/ml
Interventions	TMP-SMX 960 mg x 2 for 3 days vs TMP-SMX 960 mg x 2 for 7 days
Outcomes	Clinical cure Bacteriological cure Adverse effects
Notes	Age: 12-65
Allocation concealment	B – Unclear

Study	**Trienekens 1993**
Methods	Randomisation: the code was supplied by pharmaceutic company and was not known to the investigators, it was kept in the sealed envelopes that was broken 6 weeks after the last patient was included Blinding: double dummy technique, placebo tablets identical to active drug Intention-to-treat: no information Interim analysis: no information Excluded: 11/395 (not returned for follow-up) Follow-up: 1 week and 6 weeks (only for bacteriological cure)
Participants	The Netherlands 395 non-pregnant women Age: 18-65 Data collection: 4/89 - 10/90 Bacteriuria > 10^5 CFU/ml
Interventions	norfloxacin 400 mg x 2 for 3 days vs norfloxacin 400 mg x 2 for 7 days
Outcomes	Clinical cure Bacteriological cure Adverse effects
Notes	

Characteristics of included studies (*Continued*)

Allocation concealment	A – Adequate

Study	**Tsugawa 1999**
Methods	Randomisation: no information Blinding: double-blind Intention-to-treat: no information Interim analysis: no information Excluded for efficacy analysis: 28/99 (14 - no significant bacteriuria; 1 - withdrawal of informed consent; 2 - urinary tract infection within 4 weeks before treatment; 2 - lost for follow-up; 1 - fungi in urine before therapy; 3 - shortage of dosage; 1 - prohibited medication; 1 - anamnesis of epilepsy; 1 - 71 years or older; 1 - out of target disease) Follow-up: days 7, 14 and 35 from the treatment start
Participants	Japan 99 women Age: 20-70 Bacteriuria > 10^4 CFU/ml
Interventions	gatifloxacin 100 mg x 2 for 3 days vs gatifloxacin 100 mg x 2 for 7 days
Outcomes	Clinical cure Bacteriological cure Adverse effects
Notes	Age: 20-70
Allocation concealment	B – Unclear

Study	**Winwick 1981**
Methods	Randomisation: no information Blinding: no information Intention-to-treat: no information Interim analysis: no information Excluded: 23/81 ("not fulfilled the stipulated criteria for entry") Follow-up: 14 days after treatment start
Participants	UK 81 non-pregnant women Age : 18-65 (mean = 34) Data collection: no information Bacteriuria: no information
Interventions	nalidixic acid + sodium citrate x 3 for 3 days vs ampicillin 500 mg x 3 for 7 days
Outcomes	Bacteriological cure Adverse effects
Notes	Exact dosage of antibiotic in the 3-day group not mentioned (probably - 660 mg + 3.75 g) Different antibiotics were compared
Allocation concealment	B – Unclear

TMP = trimethoprim
SMX = sulfamethoxazole
CFU = colony-forming units

Characteristics of excluded studies

Study	Reason for exclusion
Bailey 1983	New Zealand Randomised controlled study Compares 2 treatment regimens 5 days duration both
Bargelloni 1972	Italy Not randomised controlled study Phase III trial
Blomer 1986	West Germany Not randomised controlled study Review - not systematic
Charlton 1976	UK Quasi-randomisation (alternate months)
Fair 1980	USA Quasi-randomisation (alternate patients)
Fancourt 1984	UK Randomised controlled study Inpatients only Compares 2 treatment regimens both of 7 days duration (does not include a 3-day regimen)
Furusawa 1994	Japan Not randomised controlled study Case reports
Gellerman 1988	Germany Randomised controlled study Compares single dose and three-days regimens of ciprofloxacin
Hill 1985	UK Randomised controlled study Compares 2 treatment regimens 10 days duration both (does not include a 3-day regimen)
Hoigne 1977	Switzerland Clinical controlled study Compares treatment for 2 weeks and for 4 weeks
Hooton 1989	USA Review of two randomised controlled studies : 1) comparing 2 treatment regimens of 3 days both 2) comparing 2 treatment regimens of 7 days both
Iravani 1991	USA Review of 3 different studies (only one of them - randomised controlled study and included separately)
Iravani 1995	USA Review of 3 separate studies
Ishihara 1998	Japan RCT Results - only clinical improvement and not cure
Little 1979	New Zealand Randomised controlled study Compares several treatment regimens all of wich were 5 to 7 days long (does not include a 3-day regimen)
Liudvig 1996	Germany

Characteristics of excluded studies (*Continued*)

	Not randomised controlled study
Loran 1997	Russia Not randomised controlled study (case-control study)
Martin 1983	UK Randomised controlled study Compares 2 treatment regimens both of 7 days duration (does not include a 3-day regimen)
McCarthy 1972	USA Randomised controlled study Compares 2 treatment regimens10 days duration both
Pelta 1985	UK Randomised controlled study Compares 2 treatment regimens 7 days duration both (does not include a 3-day regimen)
Raz 1996	Israel Randomised controlled study Only postmenopausal women (mean age = 66 +\- 20 years)
Schultz 1984	USA Randomised controlled study Compares single-dose with 10-days antibiotic regimens (does not include a 3-day regimen)
Vogel 1984	UK A summary of few studies comparing different regimens of 3-days therapy and 7-days therapy separately (neither comparing 3-days treatment to 7-days)
Zorbas 1995	Greece Randomised controlled study Duration of all treatment regimens - 12 weeks (does not include a 3-day regimen) Only elderly patients (mean age = 82.8 years)

ADDITIONAL TABLES

Table 01. Electronic search strategies

Database searched	Terms used
CENTRAL	#1) URINARY TRACT INFECTIONS #2) (urinary next tract next infection*) #3) uti and utis #4) bacteriuria* #5) pyuria* #6) (#1 or #2 or #3 or #4 or #5) #7) ANTI-INFECTIVE AGENTS #8) anti-infective* #9) antiinfective* #10) antibiotic* #11) quinoline* #12) cinoxacin #13) (nalidixic next acid) #14) (oxolinic next acid) #15) fluoroquinolone* #16) ciprofloxacin

Table 01. Electronic search strategies (*Continued*)

Database searched	Terms used
	#17) enoxacin #18) fleroxacin #19) norfloxacin #20) ofloxacin #21) perfloxacin #22) (#8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21) #23) (#6 and #22)
MEDLINE	1. exp Urinary Tract Infections/ 2. urinary tract infection$.tw. 3. uti.tw. 4. utis.tw. 5. pyuria.tw. 6. bacteriuria.tw. 7. or/1-6 8. exp Anti-Infective Agents/ 9. anti-infective$.tw. 10. antiinfective$.tw. 11. antibiotic$.tw. 12. antibacterial$.tw. 13. quinolone$.tw. 14. cinoxacin.tw. 15. nalidixic acid.tw. 16. oxolinic acid.tw. 17. fluoroquinolone.tw. 18. ciprofloxacin.tw. 19. enoxacin.tw. 20. fleroxacin.tw. 21. norfloxacin.tw. 22. ofloxacin.tw. 23. pefloxacin.tw. 24. or/8-23 25. 7 and 24 26. randomized controlled trial.pt. 27. controlled clinical trial.pt. 28. randomized controlled trials/ 29. random allocation/ 30. double blind method/ 31. single blind method/ 32. or/26-31 33. animal/ not (animal/ and human/) 34. 32 not 33 35. clinical trial.pt. 36. exp clinical trials/ 37. (clinic$ adj25 trial$).ti,ab. 38. cross-over studies/ 39. (crossover or cross-over or cross over).tw. 40. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab. 41. placebos/

Table 01. Electronic search strategies (*Continued*)

Database searched	Terms used
	42. placebo$.ti,ab. 43. random$.ti,ab. 44. research design/ 45. or/35-44 46. 45 not 33 47. 34 or 46 48. 25 and 47

ANALYSES

Comparison 01. Three days versus 5-10 day antibiotic therapy

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Short-term symptomatic failure (2-15 days from end of treatment)	24	5165	Relative Risk (Random) 95% CI	1.06 [0.88, 1.28]
02 Short-term symptomatic failure - ITT (2-15 days from end of treatment)	17	5029	Relative Risk (Random) 95% CI	0.98 [0.88, 1.10]
03 Long-term symptomatic failure (4-10 weeks from end of treatment)	10	3141	Relative Risk (Random) 95% CI	1.09 [0.94, 1.27]
04 Long-term symptomatic failure - ITT (4-10 weeks from end of treatment)	10	3910	Relative Risk (Random) 95% CI	1.07 [0.99, 1.16]
05 Short-term bacteriologic failure (2-15 days from end of treatment)	31	5368	Relative Risk (Random) 95% CI	1.19 [0.98, 1.44]
06 Short-term bacteriological failure by antiboitic class (same drug) (2-15 days from end of treatment)	18	3146	Relative Risk (Random) 95% CI	1.37 [1.07, 1.74]
07 Short-term bacteriological failure - ITT (2-15 days from end of treatment)	20	4163	Relative Risk (Random) 95% CI	0.92 [0.80, 1.06]
08 Long-term bacteriological failure (4-10 weeks from end of treatment)	18	3715	Relative Risk (Random) 95% CI	1.31 [1.08, 1.60]
09 Long-term bacteriological failure by antibiotic class (same drug) (4-10 weeks from end of treatment)	13	2502	Relative Risk (Random) 95% CI	1.43 [1.19, 1.73]
10 Long-term bacteriological failure - ITT (4-10 weeks from end of treatment)	13	2943	Relative Risk (Random) 95% CI	1.19 [1.06, 1.35]

11 Long-term bacteriological failure - ITT by antibiotic class (same drug) (4-10 weeks from end of treatment)	10	2127	Relative Risk (Random) 95% CI	1.26 [1.08, 1.47]
12 Patients with any adverse effects during treatment	29	7617	Relative Risk (Random) 95% CI	0.83 [0.74, 0.93]
13 Patients developed pyelonephritis	5	582	Relative Risk (Random) 95% CI	3.04 [0.32, 28.93]
14 Adverse effects requiring therapy discontinuation	24	6177	Relative Risk (Random) 95% CI	0.51 [0.28, 0.91]
15 Gastrointestinal adverse effects	24	6973	Relative Risk (Random) 95% CI	0.81 [0.67, 0.97]
16 Skin adverse effects	21	6582	Relative Risk (Random) 95% CI	0.62 [0.36, 1.06]
17 CNS adverse effects	21	5748	Relative Risk (Random) 95% CI	0.83 [0.65, 1.06]
18 Vaginal discharge as an adverse effect of therapy	18	5127	Relative Risk (Random) 95% CI	0.73 [0.49, 1.10]
19 Other adverse effects	19	5250	Relative Risk (Random) 95% CI	0.98 [0.72, 1.32]
20 Patients with any adverse effects during treatment by antibiotic class (same drug)	17	3852	Relative Risk (Random) 95% CI	0.76 [0.63, 0.92]

INDEX TERMS

Medical Subject Headings (MeSH)

Anti-Infective Agents, Urinary [*therapeutic use]; Randomized Controlled Trials; Urinary Tract Infections [*drug therapy]

MeSH check words

Female; Humans

COVER SHEET

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GRAPHS AND OTHER TABLES

Figure 01. Funnel plot - symptomatic failure

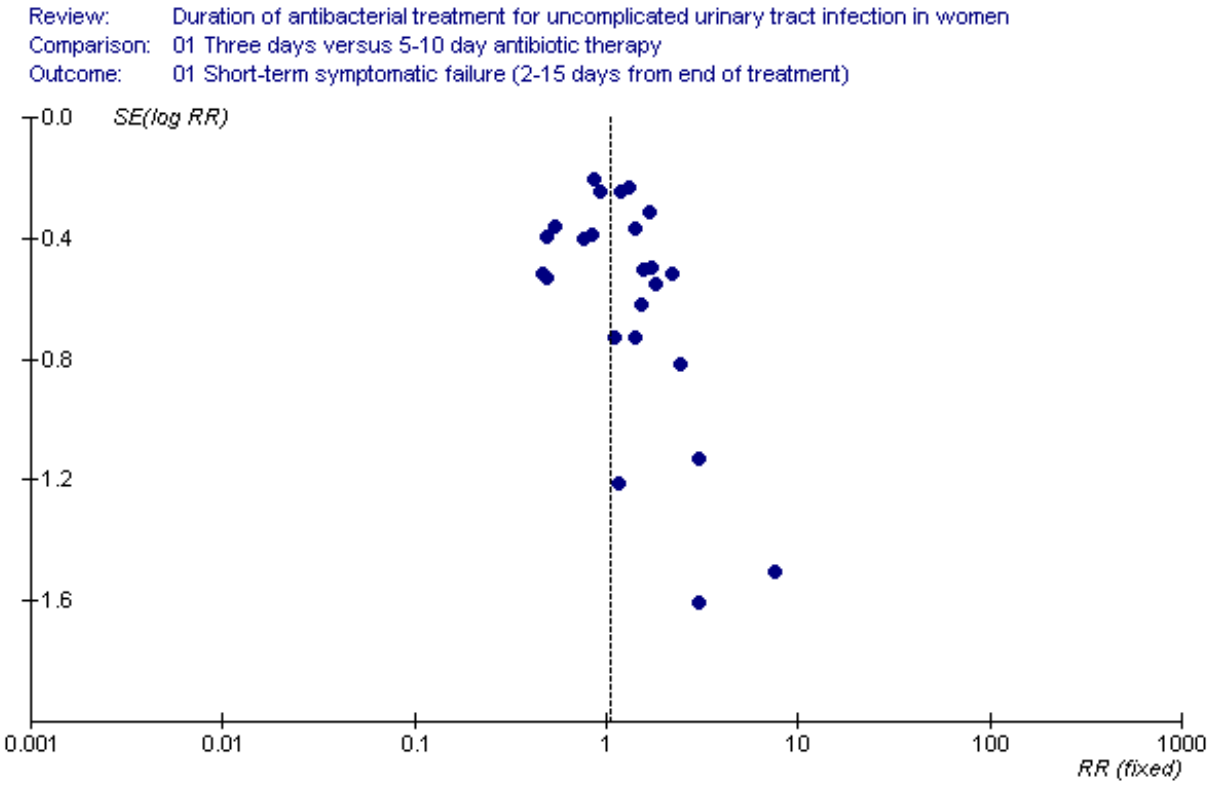
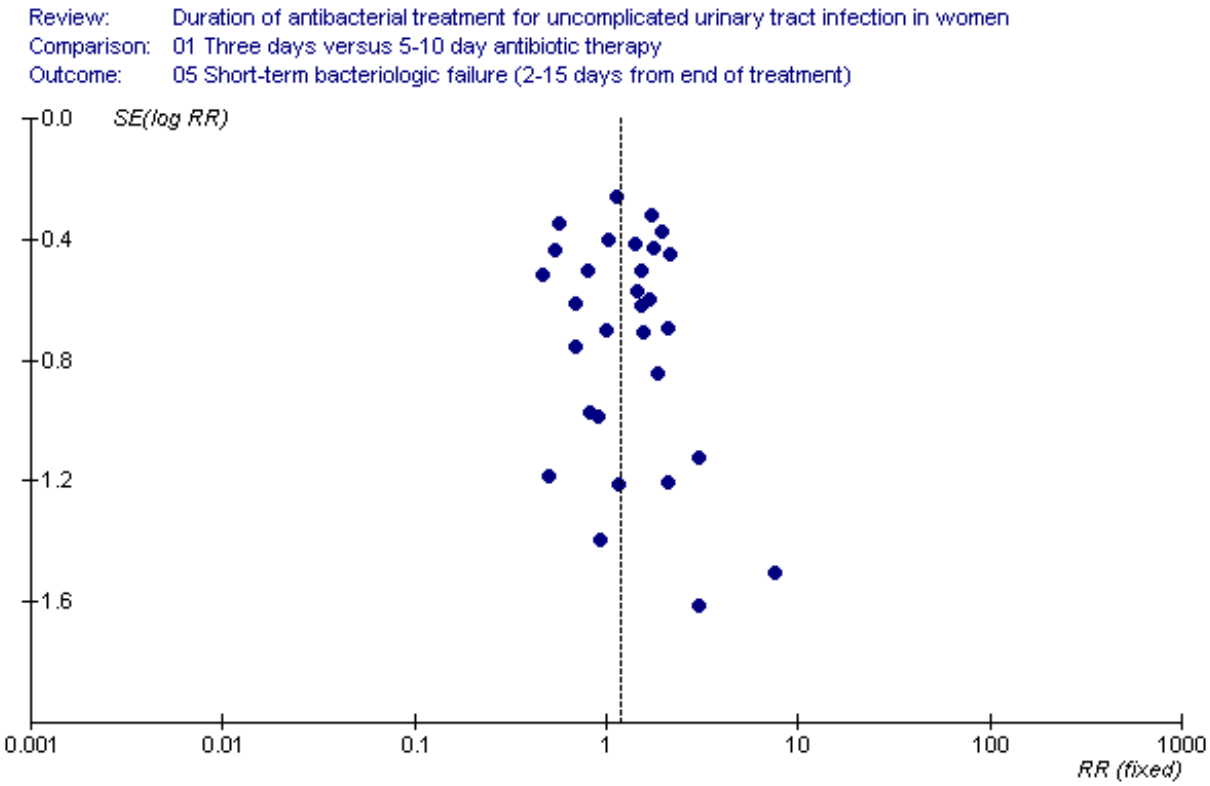


Figure 02. Funnel plot - bacteriologic failure



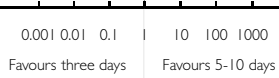
Analysis 01.01. Comparison 01 Three days versus 5-10 day antibiotic therapy, Outcome 01 Short-term symptomatic failure (2-15 days from end of treatment)

Review: Duration of antibacterial treatment for uncomplicated urinary tract infection in women

Comparison: 01 Three days versus 5-10 day antibiotic therapy

Outcome: 01 Short-term symptomatic failure (2-15 days from end of treatment)

Study	Three days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
01 Same antibiotic therapy in each group					
Garcia 2002	5/60	2/58		1.3	2.42 [0.49, 11.97]
Gossius 1984	9/91	6/95		3.1	1.57 [0.58, 4.22]
Gossius 1985	4/35	3/37		1.6	1.41 [0.34, 5.85]
Greenberg 1986	7/22	4/23		2.6	1.83 [0.62, 5.39]
Hovelius 1985	5/27	4/33		2.1	1.53 [0.45, 5.14]
Internordic 1988	38/193	27/180		10.7	1.31 [0.84, 2.06]
Iravani 1983	1/44	2/102		0.6	1.16 [0.11, 12.45]
Neringer 1992	31/196	26/196		9.7	1.19 [0.74, 1.93]
Pitkajarvi 1990	24/151	14/148		6.8	1.68 [0.90, 3.12]
Richards 1984	30/91	32/84		12.3	0.87 [0.58, 1.29]
Sandberg 1985	16/82	10/72		5.3	1.40 [0.68, 2.90]
Trienekens 1989	11/121	13/121		4.8	0.85 [0.39, 1.81]
Trienekens 1993	9/175	18/173		4.7	0.49 [0.23, 1.07]
Tsugawa 1999	3/34	1/34		0.7	3.00 [0.33, 27.42]
Subtotal (95% CI)	1322	1356		66.2	1.15 [0.95, 1.39]
Total events: 193 (Three days), 162 (5-10 days)					
Test for heterogeneity chi-square=12.18 df=13 p=0.51 I^2 =0.0%					
Test for overall effect z=1.41 p=0.2					
02 Different antibiotic therapy in each group					
Bitsch 1985	5/95	11/98		2.9	0.47 [0.17, 1.30]
Butler 1983	9/31	5/30		3.2	1.74 [0.66, 4.60]
Cox 1992	5/75	9/66		2.8	0.49 [0.17, 1.39]
Figueroa 1999	1/20	0/20		0.3	3.00 [0.13, 69.52]
Guibert 1997	11/177	19/163		5.4	0.53 [0.26, 1.09]
Henry 1999	29/374	31/369		9.6	0.92 [0.57, 1.50]
Iravani 1999	8/168	22/351		4.6	0.76 [0.35, 1.67]
Rapoport 1981	4/41	3/34		1.6	1.11 [0.27, 4.60]



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Study	Three days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Stein 1987	3/74	0/81		0.4	7.65 [0.40, 145.73]
Stein 1992	12/115	5/105		3.0	2.19 [0.80, 6.01]
Subtotal (95% CI)	1170	1317		33.8	0.90 [0.62, 1.29]
Total events: 87 (Three days), 105 (5-10 days)					
Test for heterogeneity chi-square=12.57 df=9 p=0.18 I^2 =28.4%					
Test for overall effect z=0.59 p=0.6					
Total (95% CI)	2492	2673		100.0	1.06 [0.88, 1.28]
Total events: 280 (Three days), 267 (5-10 days)					
Test for heterogeneity chi-square=27.14 df=23 p=0.25 I^2 =15.3%					
Test for overall effect z=0.65 p=0.5					

Analysis 01.02. Comparison 01 Three days versus 5-10 day antibiotic therapy, Outcome 02 Short-term symptomatic failure - ITT (2-15 days from end of treatment)

Review: Duration of antibacterial treatment for uncomplicated urinary tract infection in women

Comparison: 01 Three days versus 5-10 day antibiotic therapy

Outcome: 02 Short-term symptomatic failure - ITT (2-15 days from end of treatment)

Study	Three days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
01 Same antibiotic therapy in each group					
Greenberg 1986	10/25	7/26		2.0	1.49 [0.67, 3.29]
Internordic 1988	50/205	43/196		8.6	1.11 [0.78, 1.59]
Iravani 1983	6/49	9/109		1.3	1.48 [0.56, 3.94]
Neringer 1992	31/196	26/196		5.1	1.19 [0.74, 1.93]
Pitkajarvi 1990	24/151	14/148		3.2	1.68 [0.90, 3.12]
Richards 1984	33/94	37/89		8.1	0.84 [0.58, 1.22]
Sandberg 1985	26/92	24/86		5.3	1.01 [0.63, 1.62]
Trienekens 1989	51/161	58/166		11.0	0.91 [0.67, 1.23]
Trienekens 1993	33/199	41/196		6.7	0.79 [0.52, 1.20]
Tsugawa 1999	13/44	8/41		2.1	1.51 [0.70, 3.27]
Subtotal (95% CI)	1216	1253		53.5	1.02 [0.89, 1.18]
Total events: 277 (Three days), 267 (5-10 days)					
Test for heterogeneity chi-square=8.59 df=9 p=0.48 I^2 =0.0%					

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Study	Three days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Test for overall effect z=0.31 p=0.8					
02 Different antibiotic therapy in each group					
Cox 1992	11/81	23/82		2.9	0.48 [0.25, 0.93]
Figueroa 1999	1/20	0/20		0.1	3.00 [0.13, 69.52]
Guibert 1997	46/212	55/209		9.3	0.82 [0.59, 1.16]
Henry 1999	49/394	48/386		8.0	1.00 [0.69, 1.45]
Iravani 1999	79/239	145/474		17.3	1.08 [0.86, 1.35]
Stein 1987	3/74	0/81		0.2	7.65 [0.40, 145.73]
Stein 1992	39/142	47/146		8.6	0.85 [0.60, 1.22]
Subtotal (95% CI)	1162	1398		46.5	0.91 [0.74, 1.12]
Total events: 228 (Three days), 318 (5-10 days)					
Test for heterogeneity chi-square=8.90 df=6 p=0.18 I^2 =32.6%					
Test for overall effect z=0.89 p=0.4					
Total (95% CI)	2378	2651		100.0	0.98 [0.88, 1.10]
Total events: 505 (Three days), 585 (5-10 days)					
Test for heterogeneity chi-square=18.08 df=16 p=0.32 I^2 =11.5%					
Test for overall effect z=0.30 p=0.8					

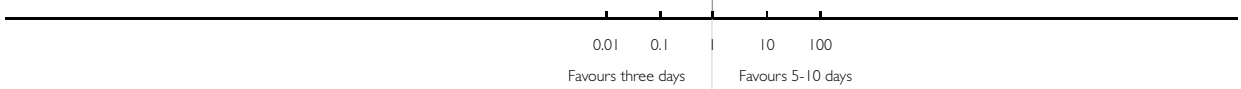
Analysis 01.03. Comparison 01 Three days versus 5-10 day antibiotic therapy, Outcome 03 Long-term symptomatic failure (4-10 weeks from end of treatment)

Review: Duration of antibacterial treatment for uncomplicated urinary tract infection in women

Comparison: 01 Three days versus 5-10 day antibiotic therapy

Outcome: 03 Long-term symptomatic failure (4-10 weeks from end of treatment)

Study	Three days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
01 Same antibiotic therapy in each group					
Internordic 1988	39/193	21/180		8.4	1.73 [1.06, 2.83]
Neringer 1992	55/196	53/196		16.7	1.04 [0.75, 1.43]
Piipo 1990	20/164	15/163		5.3	1.33 [0.70, 2.50]
Pitkajarvi 1990	41/145	28/133		11.0	1.34 [0.88, 2.04]
Sandberg 1985	35/77	28/65		13.4	1.06 [0.73, 1.53]
Trienekens 1989	19/116	17/123		5.8	1.19 [0.65, 2.17]
Trienekens 1993	19/150	28/155		7.1	0.70 [0.41, 1.20]
Tsugawa 1999	5/33	1/32		0.5	4.85 [0.60, 39.25]
Subtotal (95% CI)	1074	1047		68.2	1.16 [0.95, 1.42]
Total events: 233 (Three days), 191 (5-10 days)					
Test for heterogeneity chi-square=9.13 df=7 p=0.24 I^2 =23.3%					
Test for overall effect z=1.48 p=0.1					
02 Different antibiotic therapy in each group					
Henry 1999	75/261	82/280		22.1	0.98 [0.75, 1.28]
Iravani 1999	23/155	52/324		9.7	0.92 [0.59, 1.45]
Subtotal (95% CI)	416	604		31.8	0.97 [0.77, 1.21]
Total events: 98 (Three days), 134 (5-10 days)					
Test for heterogeneity chi-square=0.05 df=1 p=0.82 I^2 =0.0%					
Test for overall effect z=0.29 p=0.8					
Total (95% CI)	1490	1651		100.0	1.09 [0.94, 1.27]
Total events: 331 (Three days), 325 (5-10 days)					
Test for heterogeneity chi-square=10.62 df=9 p=0.30 I^2 =15.3%					
Test for overall effect z=1.13 p=0.3					



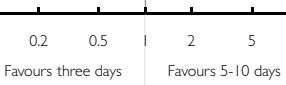
Analysis 01.04. Comparison 01 Three days versus 5-10 day antibiotic therapy, Outcome 04 Long-term symptomatic failure - ITT (4-10 weeks from end of treatment)

Review: Duration of antibacterial treatment for uncomplicated urinary tract infection in women

Comparison: 01 Three days versus 5-10 day antibiotic therapy

Outcome: 04 Long-term symptomatic failure - ITT (4-10 weeks from end of treatment)

Study	Three days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
01 Same antibiotic therapy in each group					
Internordic 1988	51/205	37/196		4.5	1.32 [0.91, 1.92]
Neringer 1992	55/196	53/196		6.2	1.04 [0.75, 1.43]
Piipo 1990	26/170	22/170		2.3	1.18 [0.70, 2.00]
Pitkajarvi 1990	47/151	43/148		5.3	1.07 [0.76, 1.51]
Sandberg 1985	50/92	49/86		9.3	0.95 [0.73, 1.24]
Trienekens 1989	64/161	60/166		8.3	1.10 [0.83, 1.45]
Trienekens 1993	68/199	69/196		8.7	0.97 [0.74, 1.27]
Tsugawa 1999	17/44	10/41		1.5	1.58 [0.82, 3.05]
Subtotal (95% CI)	1218	1199		46.1	1.07 [0.95, 1.20]
Total events: 378 (Three days), 343 (5-10 days)					
Test for heterogeneity chi-square=4.06 df=7 p=0.77 I^2 =0.0%					
Test for overall effect z=1.09 p=0.3					
02 Different antibiotic therapy in each group					
Henry 1999	208/394	188/386		33.2	1.08 [0.94, 1.25]
Iravani 1999	107/239	202/474		20.7	1.05 [0.88, 1.25]
Subtotal (95% CI)	633	860		53.9	1.07 [0.96, 1.19]
Total events: 315 (Three days), 390 (5-10 days)					
Test for heterogeneity chi-square=0.08 df=1 p=0.78 I^2 =0.0%					
Test for overall effect z=1.24 p=0.2					
Total (95% CI)	1851	2059		100.0	1.07 [0.99, 1.16]
Total events: 693 (Three days), 733 (5-10 days)					
Test for heterogeneity chi-square=4.11 df=9 p=0.90 I^2 =0.0%					
Test for overall effect z=1.64 p=0.1					



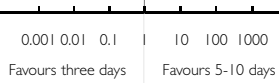
Analysis 01.05. Comparison 01 Three days versus 5-10 day antibiotic therapy, Outcome 05 Short-term bacteriologic failure (2-15 days from end of treatment)

Review: Duration of antibacterial treatment for uncomplicated urinary tract infection in women

Comparison: 01 Three days versus 5-10 day antibiotic therapy

Outcome: 05 Short-term bacteriologic failure (2-15 days from end of treatment)

Study	Three days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
01 Same antibiotic therapy in each group					
Garcia 2002	7/60	4/58		2.6	1.69 [0.52, 5.47]
Gordin 1987a	1/32	1/30		0.5	0.94 [0.06, 14.33]
Gordin 1987b	6/36	7/34		3.8	0.81 [0.30, 2.17]
Gossius 1984	6/91	3/95		2.0	2.09 [0.54, 8.10]
Gossius 1985	2/35	1/37		0.7	2.11 [0.20, 22.29]
Greenberg 1986	7/22	5/24		3.7	1.53 [0.57, 4.12]
Hansen 1981	7/102	15/119		4.9	0.54 [0.23, 1.28]
Hovelius 1985	5/27	4/33		2.5	1.53 [0.45, 5.14]
Internordic 1988	12/193	11/180		5.8	1.02 [0.46, 2.25]
Iravani 1983	1/44	2/102		0.6	1.16 [0.11, 12.45]
Marsh 1980	5/22	5/32		2.9	1.45 [0.48, 4.43]
Neringer 1992	24/196	14/196		9.2	1.71 [0.91, 3.21]
Piipo 1990	4/163	4/162		1.9	0.99 [0.25, 3.91]
Pitkajarvi 1990	13/151	9/148		5.4	1.42 [0.62, 3.21]
Richards 1984	4/22	3/26		1.9	1.58 [0.39, 6.30]
Trienekens 1989	19/132	10/136		6.9	1.96 [0.95, 4.05]
Trienekens 1993	14/169	8/169		5.1	1.75 [0.75, 4.06]
Tsugawa 1999	1/34	0/34		0.4	3.00 [0.13, 71.15]
Subtotal (95% CI)	1531	1615		60.8	1.37 [1.07, 1.74]
Total events: 138 (Three days), 106 (5-10 days)					
Test for heterogeneity chi-square=9.13 df=17 p=0.94 I^2 =0.0%					
Test for overall effect z=2.50 p=0.01					
02 Different antibiotic therapy in each group					
Basista 1991	4/29	5/25		2.5	0.69 [0.21, 2.29]
Bitsch 1985	5/95	11/98		3.5	0.47 [0.17, 1.30]
Butler 1983	3/27	1/27		0.8	3.00 [0.33, 27.06]
Cox 1992	2/75	2/68		1.0	0.91 [0.13, 6.26]



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Study	Three days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Figueroa 1999	1/20	2/20		0.7	0.50 [0.05, 5.08]
Henry 1999	15/203	7/203		4.7	2.14 [0.89, 5.14]
Hooton 1991	4/48	2/44		1.3	1.83 [0.35, 9.52]
Iravani 1999	20/168	37/351		13.9	1.13 [0.68, 1.88]
Menday 2000	11/107	20/109		7.7	0.56 [0.28, 1.11]
Rapoport 1981	2/41	2/34		1.0	0.83 [0.12, 5.58]
Stein 1987	3/74	0/81		0.4	7.65 [0.40, 145.73]
Stein 1992	3/115	4/105		1.7	0.68 [0.16, 2.99]
× Winwick 1981	0/29	0/26		0.0	Not estimable
Subtotal (95% CI)	1031	1191		39.2	0.96 [0.68, 1.35]
Total events: 73 (Three days), 93 (5-10 days)					
Test for heterogeneity chi-square=12.28 df=11 p=0.34 I^2 =10.4%					
Test for overall effect z=0.26 p=0.8					
Total (95% CI)	2562	2806		100.0	1.19 [0.98, 1.44]
Total events: 211 (Three days), 199 (5-10 days)					
Test for heterogeneity chi-square=24.54 df=29 p=0.70 I^2 =0.0%					
Test for overall effect z=1.78 p=0.08					

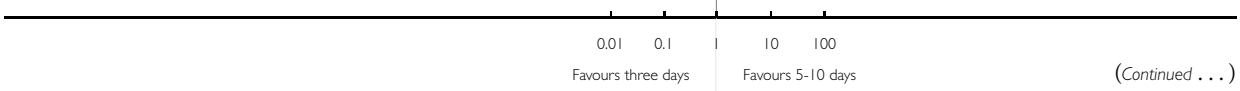
Analysis 01.06. Comparison 01 Three days versus 5-10 day antibiotic therapy, Outcome 06 Short-term bacteriological failure by antiboitic class (same drug) (2-15 days from end of treatment)

Review: Duration of antibacterial treatment for uncomplicated urinary tract infection in women

Comparison: 01 Three days versus 5-10 day antibiotic therapy

Outcome: 06 Short-term bacteriological failure by antiboitic class (same drug) (2-15 days from end of treatment)

Study	Three days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
01 Quinolones					
Garcia 2002	7/60	4/58		4.3	1.69 [0.52, 5.47]
Internordic 1988	12/193	11/180		9.5	1.02 [0.46, 2.25]
Neringer 1992	24/196	14/196		15.1	1.71 [0.91, 3.21]
Piipo 1990	4/163	4/162		3.2	0.99 [0.25, 3.91]
Trienekens 1993	14/169	8/169		8.4	1.75 [0.75, 4.06]
Tsugawa 1999	1/34	0/34		0.6	3.00 [0.13, 71.15]
Subtotal (95% CI)	815	799		41.2	1.47 [1.01, 2.16]
Total events: 62 (Three days), 41 (5-10 days)					
Test for heterogeneity chi-square=1.79 df=5 p=0.88 I^2 =0.0%					
Test for overall effect z=1.99 p=0.05					
02 Beta-lactams					
Gordin 1987b	6/36	7/34		6.2	0.81 [0.30, 2.17]
Greenberg 1986	7/22	5/24		6.1	1.53 [0.57, 4.12]
Hansen 1981	7/102	15/119		8.1	0.54 [0.23, 1.28]
Hovelius 1985	5/27	4/33		4.1	1.53 [0.45, 5.14]
Marsh 1980	5/22	5/32		4.8	1.45 [0.48, 4.43]
Pitkajarvi 1990	13/151	9/148		8.9	1.42 [0.62, 3.21]
Richards 1984	4/22	3/26		3.1	1.58 [0.39, 6.30]
Subtotal (95% CI)	382	416		41.3	1.11 [0.76, 1.63]
Total events: 47 (Three days), 48 (5-10 days)					
Test for heterogeneity chi-square=4.54 df=6 p=0.60 I^2 =0.0%					
Test for overall effect z=0.55 p=0.6					
03 TMP/sulfonamides					
Gordin 1987a	1/32	1/30		0.8	0.94 [0.06, 14.33]
Gossius 1984	6/91	3/95		3.3	2.09 [0.54, 8.10]
Gossius 1985	2/35	1/37		1.1	2.11 [0.20, 22.29]
Iravani 1983	1/44	2/102		1.1	1.16 [0.11, 12.45]
Trienekens 1989	19/132	10/136		11.3	1.96 [0.95, 4.05]



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Study	Three days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Subtotal (95% CI)	334	400		17.5	1.86 [1.04, 3.34]
Total events: 29 (Three days), 17 (5-10 days)					
Test for heterogeneity chi-square=0.45 df=4 p=0.98 I^2 =0.0%					
Test for overall effect z=2.09 p=0.04					
Total (95% CI)	1531	1615		100.0	1.37 [1.07, 1.74]
Total events: 138 (Three days), 106 (5-10 days)					
Test for heterogeneity chi-square=9.13 df=17 p=0.94 I^2 =0.0%					
Test for overall effect z=2.50 p=0.01					

Analysis 01.07. Comparison 01 Three days versus 5-10 day antibiotic therapy, Outcome 07 Short-term bacteriological failure - ITT (2-15 days from end of treatment)

Review: Duration of antibacterial treatment for uncomplicated urinary tract infection in women

Comparison: 01 Three days versus 5-10 day antibiotic therapy

Outcome: 07 Short-term bacteriological failure - ITT (2-15 days from end of treatment)

Study	Three days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
01 Same antibiotic therapy in each group					
Gordin 1987a	2/33	6/35		0.8	0.35 [0.08, 1.63]
Gordin 1987b	6/36	8/35		2.1	0.73 [0.28, 1.89]
Greenberg 1986	10/25	7/26		2.9	1.49 [0.67, 3.29]
Hansen 1981	7/102	15/119		2.6	0.54 [0.23, 1.28]
Hovelius 1985	5/27	4/33		1.3	1.53 [0.45, 5.14]
Internordic 1988	24/205	27/196		6.5	0.85 [0.51, 1.42]
Iravani 1983	6/49	9/109		2.0	1.48 [0.56, 3.94]
Neringer 1992	24/196	14/196		4.5	1.71 [0.91, 3.21]
Piipo 1990	11/170	12/170		3.0	0.92 [0.42, 2.02]
Pitkajarvi 1990	13/151	9/148		2.8	1.42 [0.62, 3.21]
Trienekens 1989	48/161	49/166		12.9	1.01 [0.72, 1.41]
Tsugawa 1999	11/44	7/41		2.6	1.46 [0.63, 3.41]
Subtotal (95% CI)	1199	1274		44.0	1.06 [0.87, 1.29]
Total events: 167 (Three days), 167 (5-10 days)					
Test for heterogeneity chi-square=10.61 df=11 p=0.48 I^2 =0.0%					

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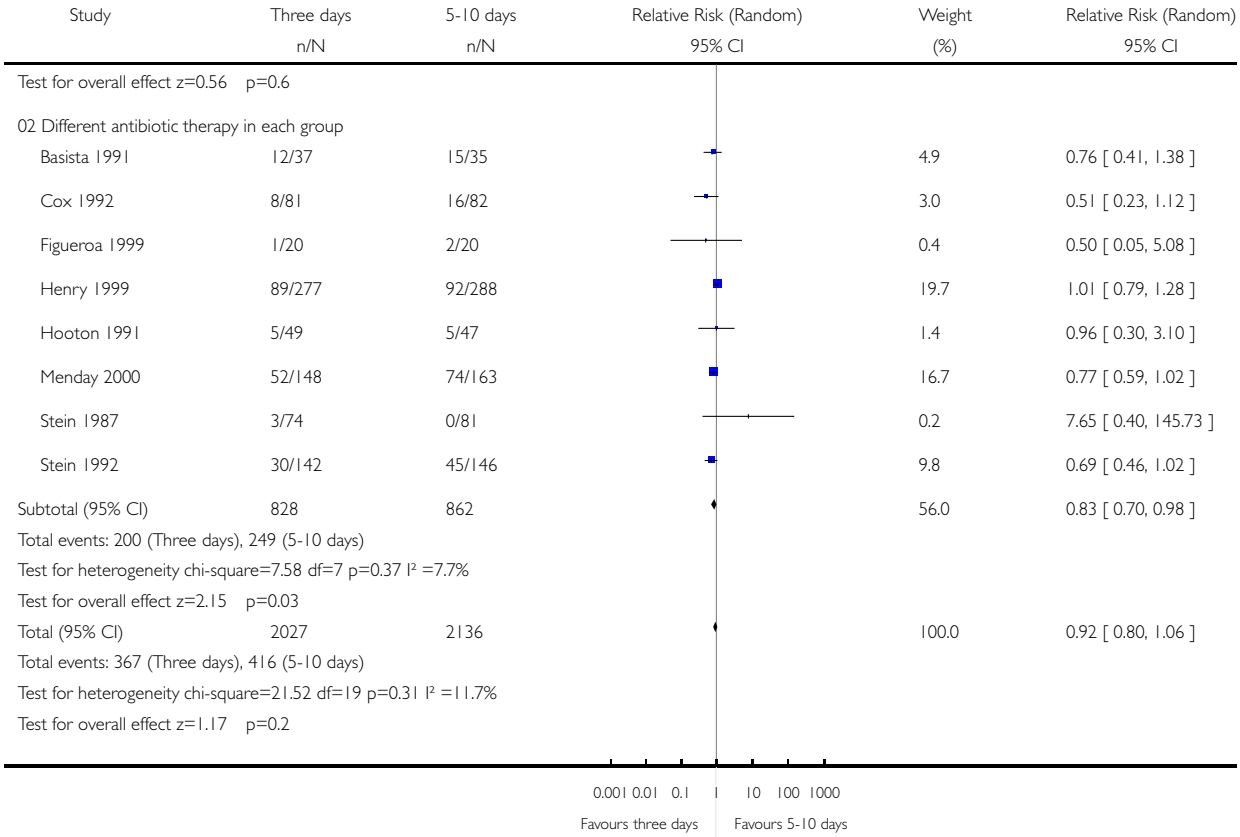
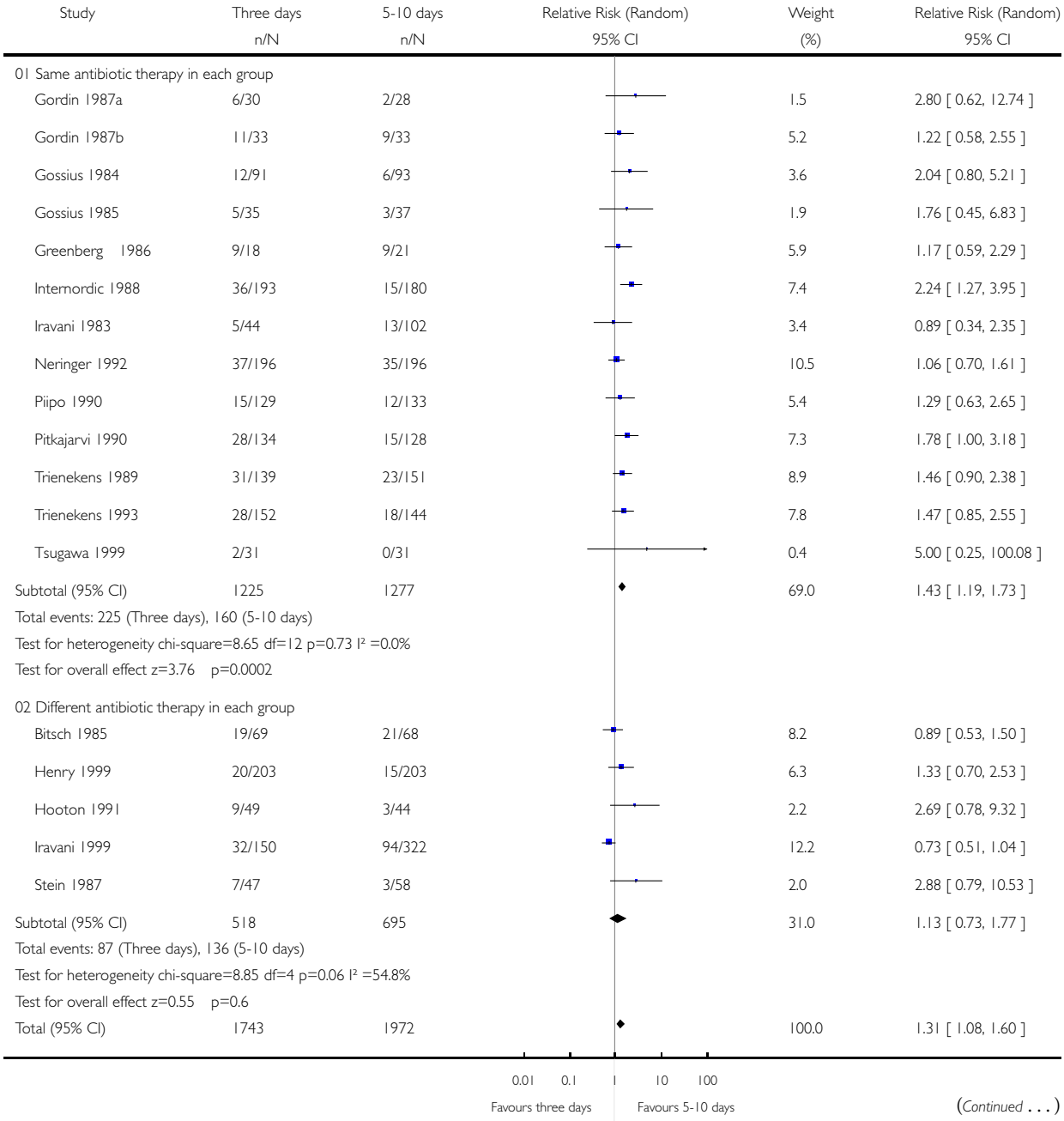


Analysis 01.08. Comparison 01 Three days versus 5-10 day antibiotic therapy, Outcome 08 Long-term bacteriological failure (4-10 weeks from end of treatment)

Review: Duration of antibacterial treatment for uncomplicated urinary tract infection in women

Comparison: 01 Three days versus 5-10 day antibiotic therapy

Outcome: 08 Long-term bacteriological failure (4-10 weeks from end of treatment)



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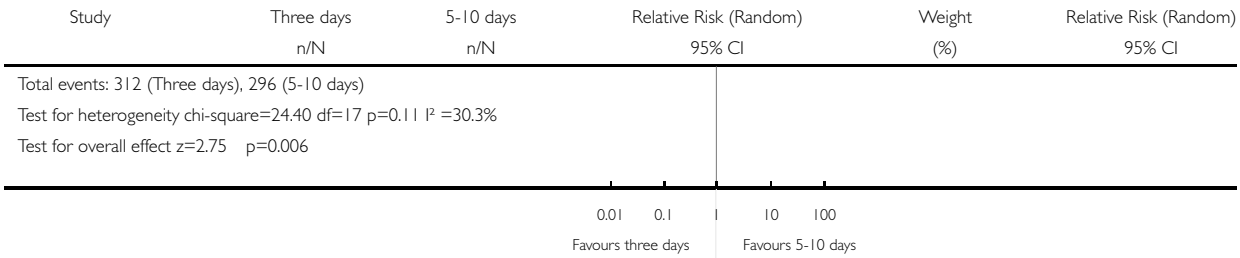


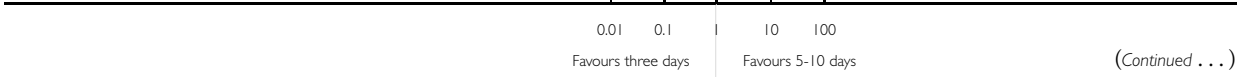
Analysis 01.09. Comparison 01 Three days versus 5-10 day antibiotic therapy, Outcome 09 Long-term bacteriological failure by antibiotic class (same drug) (4-10 weeks from end of treatment)

Review: Duration of antibacterial treatment for uncomplicated urinary tract infection in women

Comparison: 01 Three days versus 5-10 day antibiotic therapy

Outcome: 09 Long-term bacteriological failure by antibiotic class (same drug) (4-10 weeks from end of treatment)

Study	Three days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
01 Quinolones					
Internordic 1988	36/193	15/180		10.9	2.24 [1.27, 3.95]
Neringer 1992	37/196	35/196		20.0	1.06 [0.70, 1.61]
Piipo 1990	15/129	12/133		6.7	1.29 [0.63, 2.65]
Trienekens 1993	28/152	18/144		11.7	1.47 [0.85, 2.55]
Tsugawa 1999	2/31	0/31		0.4	5.00 [0.25, 100.08]
Subtotal (95% CI)	701	684		49.7	1.43 [1.04, 1.97]
Total events: 118 (Three days), 80 (5-10 days)					
Test for heterogeneity chi-square=5.18 df=4 p=0.27 I² =22.8%					
Test for overall effect z=2.22 p=0.03					
02 Beta-lactams					
Gordin 1987b	11/33	9/33		6.4	1.22 [0.58, 2.55]
Greenberg 1986	9/18	9/21		7.6	1.17 [0.59, 2.29]
Pitkajarvi 1990	28/134	15/128		10.4	1.78 [1.00, 3.18]
Subtotal (95% CI)	185	182		24.5	1.41 [0.97, 2.06]
Total events: 48 (Three days), 33 (5-10 days)					
Test for heterogeneity chi-square=1.12 df=2 p=0.57 I² =0.0%					
Test for overall effect z=1.80 p=0.07					
03 TMP/sulfonamides					
Gordin 1987a	6/30	2/28		1.5	2.80 [0.62, 12.74]
Gossius 1984	12/91	6/93		4.0	2.04 [0.80, 5.21]



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Study	Three days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Gossius 1985	5/35	3/37		1.9	1.76 [0.45, 6.83]
Iravani 1983	5/44	13/102		3.7	0.89 [0.34, 2.35]
Trienekens 1989	31/139	23/151		14.7	1.46 [0.90, 2.38]
Subtotal (95% CI)	339	411		25.8	1.51 [1.05, 2.18]
Total events: 59 (Three days), 47 (5-10 days)					
Test for heterogeneity chi-square=2.24 df=4 p=0.69 I^2 =0.0%					
Test for overall effect z=2.20 p=0.03					
Total (95% CI)	1225	1277		100.0	1.43 [1.19, 1.73]
Total events: 225 (Three days), 160 (5-10 days)					
Test for heterogeneity chi-square=8.65 df=12 p=0.73 I^2 =0.0%					
Test for overall effect z=3.76 p=0.0002					

Analysis 01.10. Comparison 01 Three days versus 5-10 day antibiotic therapy, Outcome 10 Long-term bacteriological failure - ITT (4-10 weeks from end of treatment)

Review: Duration of antibacterial treatment for uncomplicated urinary tract infection in women

Comparison: 01 Three days versus 5-10 day antibiotic therapy

Outcome: 10 Long-term bacteriological failure - ITT (4-10 weeks from end of treatment)

Study	Three days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
01 Same antibiotic therapy in each group					
Gordin 1987a	9/33	9/35		2.3	1.06 [0.48, 2.34]
Gordin 1987b	14/36	11/35		3.6	1.24 [0.65, 2.34]
Greenberg 1986	16/25	13/26		6.2	1.28 [0.79, 2.08]
Internordic 1988	48/205	31/196		8.7	1.48 [0.99, 2.22]
Iravani 1983	10/49	20/109		3.1	1.11 [0.56, 2.20]
Neringer 1992	37/196	35/196		8.3	1.06 [0.70, 1.61]
Piipo 1990	21/135	19/140		4.4	1.15 [0.65, 2.03]
Pitkajarvi 1990	45/151	35/148		10.1	1.26 [0.86, 1.84]
Trienekens 1989	53/161	38/166		11.4	1.44 [1.01, 2.05]
Tsugawa 1999	12/44	10/41		2.8	1.12 [0.54, 2.30]
Subtotal (95% CI)	1035	1092		60.9	1.26 [1.08, 1.47]

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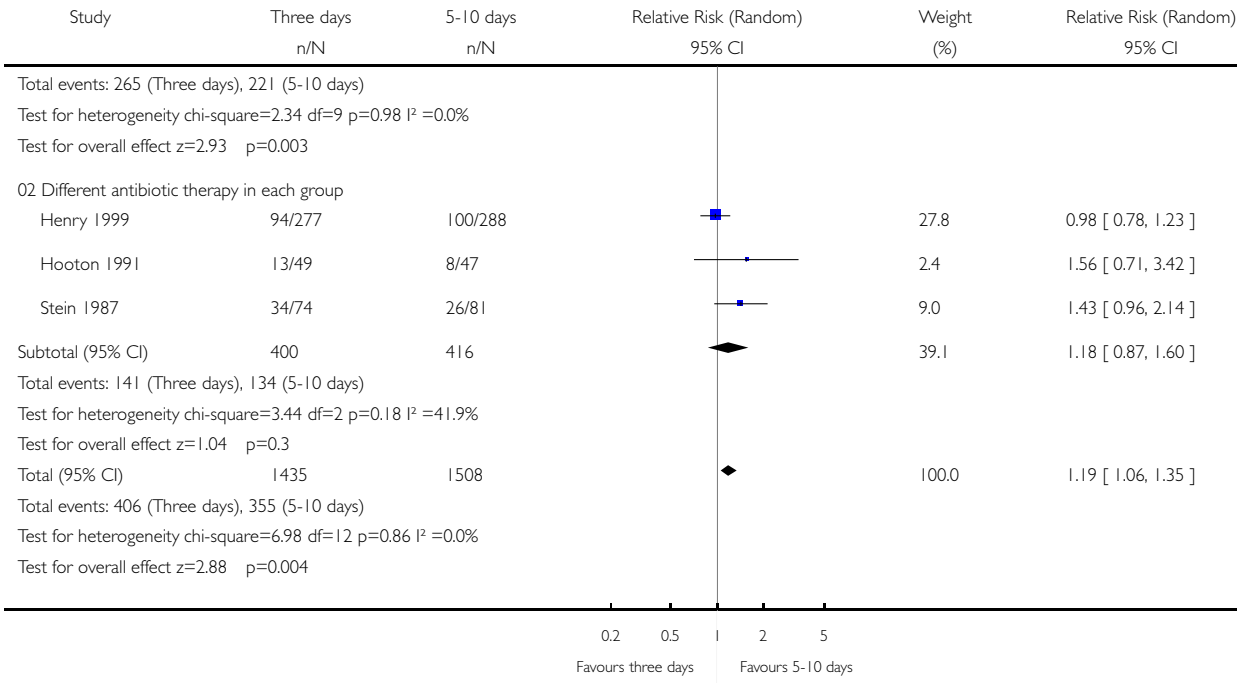
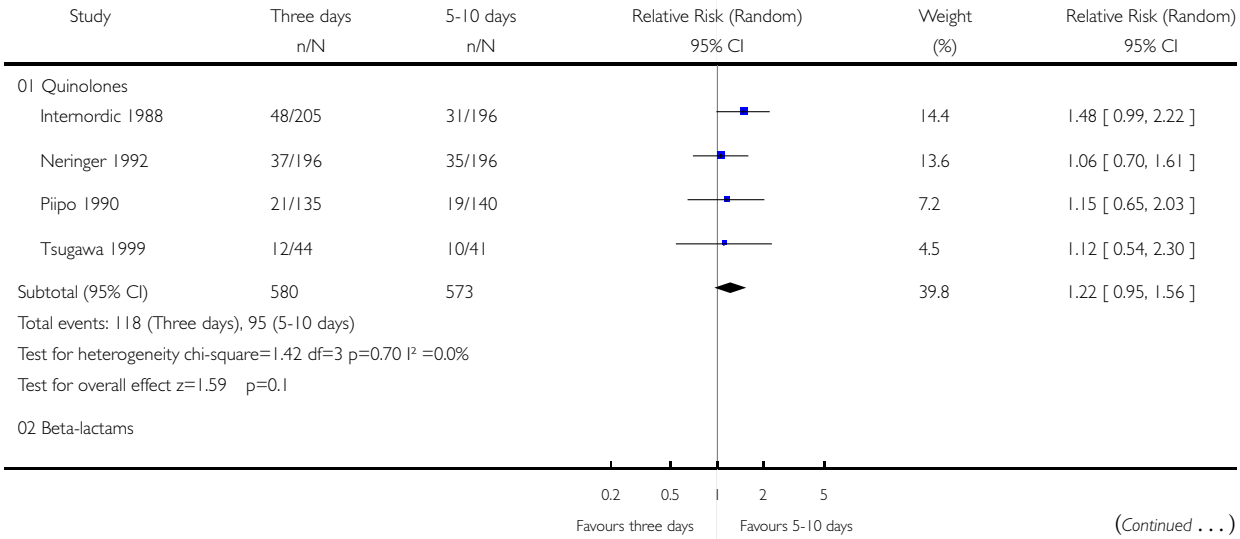


Analysis 01.11. Comparison 01 Three days versus 5-10 day antibiotic therapy, Outcome 11 Long-term bacteriological failure - ITT by antibiotic class (same drug) (4-10 weeks from end of treatment)

Review: Duration of antibacterial treatment for uncomplicated urinary tract infection in women

Comparison: 01 Three days versus 5-10 day antibiotic therapy

Outcome: 11 Long-term bacteriological failure - ITT by antibiotic class (same drug) (4-10 weeks from end of treatment)



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Study	Three days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Gordin 1987b	14/36	11/35		5.8	1.24 [0.65, 2.34]
Greenberg 1986	16/25	13/26		10.2	1.28 [0.79, 2.08]
Pitkajarvi 1990	45/151	35/148		16.5	1.26 [0.86, 1.84]
Subtotal (95% CI)	212	209		32.5	1.26 [0.96, 1.65]
Total events: 75 (Three days), 59 (5-10 days)					
Test for heterogeneity chi-square=0.01 df=2 p=1.00 I^2 =0.0%					
Test for overall effect z=1.69 p=0.09					
03 TMP/sulfonamides					
Gordin 1987a	9/33	9/35		3.8	1.06 [0.48, 2.34]
Iravani 1983	10/49	20/109		5.1	1.11 [0.56, 2.20]
Trienekens 1989	53/161	38/166		18.8	1.44 [1.01, 2.05]
Subtotal (95% CI)	243	310		27.7	1.32 [0.98, 1.76]
Total events: 72 (Three days), 67 (5-10 days)					
Test for heterogeneity chi-square=0.76 df=2 p=0.68 I^2 =0.0%					
Test for overall effect z=1.83 p=0.07					
Total (95% CI)	1035	1092		100.0	1.26 [1.08, 1.47]
Total events: 265 (Three days), 221 (5-10 days)					
Test for heterogeneity chi-square=2.34 df=9 p=0.98 I^2 =0.0%					
Test for overall effect z=2.93 p=0.003					

Analysis 01.12. Comparison 01 Three days versus 5-10 day antibiotic therapy, Outcome 12 Patients with any adverse effects during treatment

Review: Duration of antibacterial treatment for uncomplicated urinary tract infection in women

Comparison: 01 Three days versus 5-10 day antibiotic therapy

Outcome: 12 Patients with any adverse effects during treatment

Study	Three days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
01 Same antibiotic therapy in each group					
Gordin 1987a	0/32	5/30		0.2	0.09 [0.00, 1.48]
Gordin 1987b	2/36	3/34		0.4	0.63 [0.11, 3.54]
Gossius 1984	12/136	37/132		3.0	0.31 [0.17, 0.58]
Gossius 1985	4/50	18/64		1.1	0.28 [0.10, 0.79]
Greenberg 1986	0/26	1/28		0.1	0.36 [0.02, 8.42]
Hansen 1981	3/102	7/119		0.7	0.50 [0.13, 1.88]
Hovelius 1985	2/27	1/33		0.2	2.44 [0.23, 25.53]
Internordic 1988	46/239	58/240		7.7	0.80 [0.57, 1.12]
Marsh 1980	17/59	22/69		3.8	0.90 [0.53, 1.53]
Neringer 1992	57/228	73/235		9.5	0.80 [0.60, 1.08]
Piipo 1990	28/197	22/197		3.9	1.27 [0.75, 2.15]
Pitkajarvi 1990	21/174	20/171		3.3	1.03 [0.58, 1.83]
Richards 1984	8/92	15/86		1.8	0.50 [0.22, 1.12]
Sandberg 1985	10/102	12/100		1.8	0.82 [0.37, 1.80]
Trienekens 1989	40/161	51/166		7.4	0.81 [0.57, 1.15]
Trienekens 1993	26/199	29/193		4.4	0.87 [0.53, 1.42]
Tsugawa 1999	4/45	5/50		0.8	0.89 [0.25, 3.11]
Subtotal (95% CI)	1905	1947		50.1	0.76 [0.63, 0.92]
Total events: 280 (Three days), 379 (5-10 days)					
Test for heterogeneity chi-square=22.63 df=16 p=0.12 I^2 =29.3%					
Test for overall effect z=2.87 p=0.004					
02 Different antibiotic therapy in each group					
Basista 1991	5/49	9/45		1.2	0.51 [0.18, 1.41]
Bitsch 1985	6/158	5/152		0.9	1.15 [0.36, 3.70]
Cox 1992	14/101	19/99		2.8	0.72 [0.38, 1.36]
× Figueroa 1999	0/20	0/20		0.0	Not estimable
Guibert 1997	33/212	34/209		5.2	0.96 [0.62, 1.48]

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Study	Three days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Henry 1999	119/394	106/386		13.3	1.10 [0.88, 1.37]
Hooton 1991	16/49	19/47		3.8	0.81 [0.47, 1.37]
Iravani 1999	68/239	170/474		12.5	0.79 [0.63, 1.00]
Menday 2000	13/219	16/221		2.3	0.82 [0.40, 1.66]
Stein 1987	15/109	15/100		2.6	0.92 [0.47, 1.78]
Stein 1992	24/197	31/207		4.3	0.81 [0.50, 1.34]
Winwick 1981	6/30	6/28		1.2	0.93 [0.34, 2.56]
Subtotal (95% CI)	1777	1988		49.9	0.90 [0.80, 1.03]
Total events: 319 (Three days), 430 (5-10 days)					
Test for heterogeneity chi-square=6.59 df=10 p=0.76 I^2 =0.0%					
Test for overall effect z=1.53 p=0.1					
Total (95% CI)	3682	3935		100.0	0.83 [0.74, 0.93]
Total events: 599 (Three days), 809 (5-10 days)					
Test for heterogeneity chi-square=31.55 df=27 p=0.25 I^2 =14.4%					
Test for overall effect z=3.30 p=0.001					

Analysis 01.13. Comparison 01 Three days versus 5-10 day antibiotic therapy, Outcome 13 Patients developed pyelonephritis

Review: Duration of antibacterial treatment for uncomplicated urinary tract infection in women

Comparison: 01 Three days versus 5-10 day antibiotic therapy

Outcome: 13 Patients developed pyelonephritis

Study	Three days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
01 Same antibiotic therapy in each group					
Gossius 1984	1/91	0/95		49.9	3.13 [0.13, 75.87]
Gossius 1985	1/68	0/67		50.1	2.96 [0.12, 71.31]
× Hovelius 1985	0/27	0/33		0.0	Not estimable
Subtotal (95% CI)	186	195		100.0	3.04 [0.32, 28.93]
Total events: 2 (Three days), 0 (5-10 days)					
Test for heterogeneity chi-square=0.00 df=1 p=0.98 I^2 =0.0%					
Test for overall effect z=0.97 p=0.3					
02 Different antibiotic therapy in each group					

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Study	Three days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
× Cox 1992	0/75	0/68		0.0	Not estimable
× Winwick 1981	0/30	0/28		0.0	Not estimable
Subtotal (95% CI)	105	96		0.0	Not estimable
Total events: 0 (Three days), 0 (5-10 days)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
Total (95% CI)	291	291		100.0	3.04 [0.32, 28.93]
Total events: 2 (Three days), 0 (5-10 days)					
Test for heterogeneity chi-square=0.00 df=1 p=0.98 I^2 =0.0%					
Test for overall effect z=0.97 p=0.3					

Analysis 01.14. Comparison 01 Three days versus 5-10 day antibiotic therapy, Outcome 14 Adverse effects requiring therapy discontinuation

Review: Duration of antibacterial treatment for uncomplicated urinary tract infection in women

Comparison: 01 Three days versus 5-10 day antibiotic therapy

Outcome: 14 Adverse effects requiring therapy discontinuation

Study	Three days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
01 Same antibiotic therapy in each group					
Gordin 1987a	0/32	3/30		3.2	0.13 [0.01, 2.49]
× Gordin 1987b	0/36	0/34		0.0	Not estimable
Gossius 1984	0/136	20/132		3.4	0.02 [0.00, 0.39]
Gossius 1985	1/50	9/64		5.4	0.14 [0.02, 1.09]
× Greenberg 1986	0/26	0/28		0.0	Not estimable
× Hovelius 1985	0/27	0/33		0.0	Not estimable
Internordic 1988	6/239	5/240		9.5	1.21 [0.37, 3.90]
Marsh 1980	1/59	2/69		4.3	0.58 [0.05, 6.29]
Neringer 1992	2/228	14/235		7.8	0.15 [0.03, 0.64]
Piipo 1990	5/197	0/197		3.2	11.00 [0.61, 197.60]
× Pitkajarvi 1990	0/174	0/171		0.0	Not estimable
Richards 1984	1/92	2/86		4.3	0.47 [0.04, 5.06]

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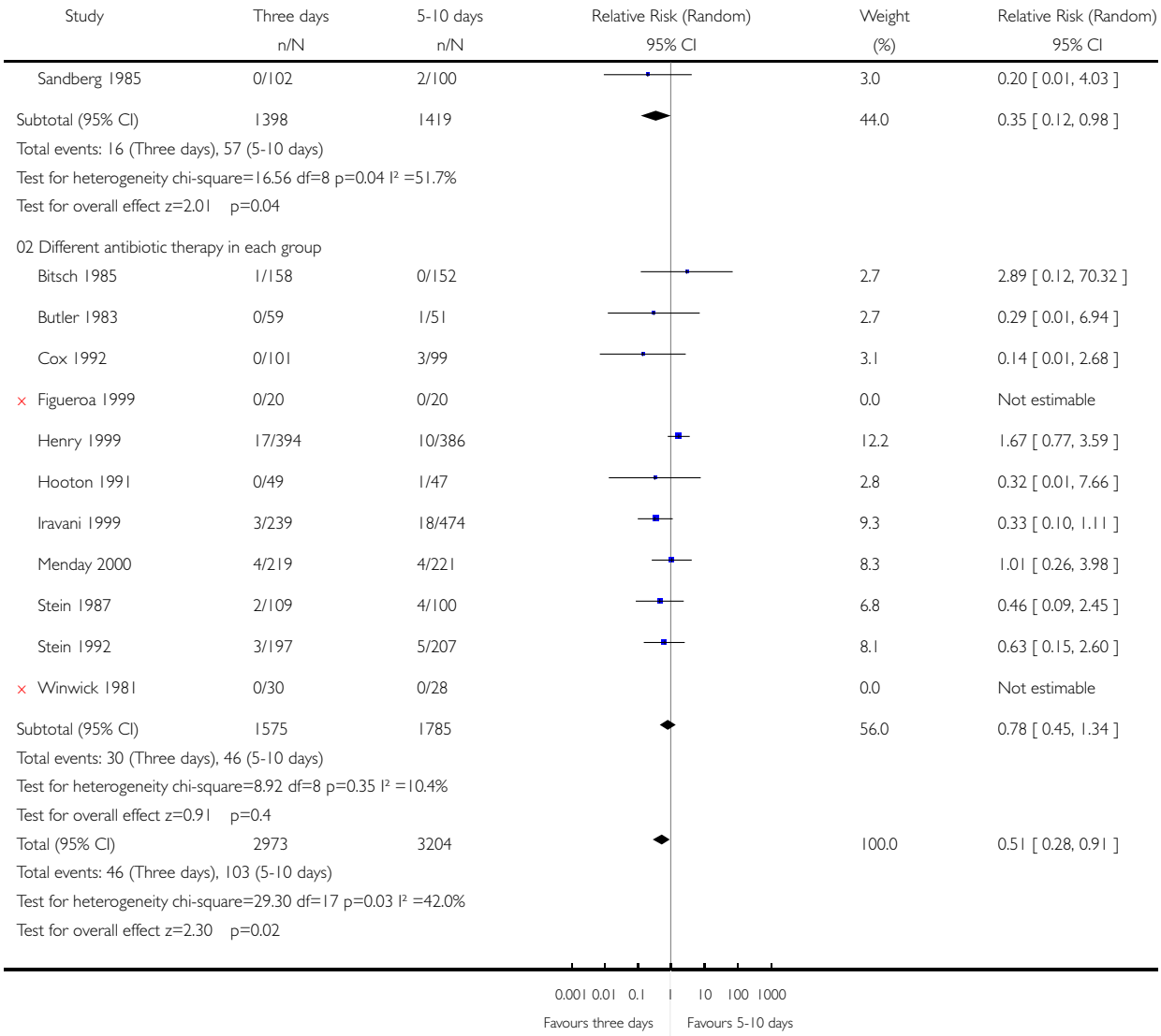

Analysis 01.15. Comparison 01 Three days versus 5-10 day antibiotic therapy, Outcome 15 Gastrointestinal adverse effects

Review: Duration of antibacterial treatment for uncomplicated urinary tract infection in women

Comparison: 01 Three days versus 5-10 day antibiotic therapy

Outcome: 15 Gastrointestinal adverse effects

Study	Three days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
01 Same antibiotic therapy in each group					
Gordin 1987a	0/32	1/30		0.3	0.31 [0.01, 7.40]
× Gordin 1987b	0/36	0/34		0.0	Not estimable
Gossius 1984	6/136	11/132		3.5	0.53 [0.20, 1.39]
Gossius 1985	3/50	7/64		2.0	0.55 [0.15, 2.01]
× Greenberg 1986	0/26	0/28		0.0	Not estimable
Hansen 1981	3/102	7/119		1.9	0.50 [0.13, 1.88]
Internordic 1988	24/239	26/240		9.8	0.93 [0.55, 1.57]
Marsh 1980	9/59	13/69		5.1	0.81 [0.37, 1.76]
Neringer 1992	11/228	19/235		5.9	0.60 [0.29, 1.23]
Piipo 1990	17/197	11/197		5.7	1.55 [0.74, 3.21]
Pitkajarvi 1990	8/174	6/171		3.0	1.31 [0.46, 3.70]
Richards 1984	5/92	9/86		3.0	0.52 [0.18, 1.49]
Sandberg 1985	4/102	6/100		2.2	0.65 [0.19, 2.25]
Trienekens 1989	22/161	34/166		10.9	0.67 [0.41, 1.09]
Tsugawa 1999	2/45	3/50		1.1	0.74 [0.13, 4.23]
Subtotal (95% CI)	1679	1721		54.4	0.77 [0.61, 0.97]
Total events: 114 (Three days), 153 (5-10 days)					
Test for heterogeneity chi-square=7.96 df=12 p=0.79 I^2 =0.0%					
Test for overall effect z=2.17 p=0.03					
02 Different antibiotic therapy in each group					
Bitsch 1985	6/158	3/152		1.8	1.92 [0.49, 7.56]
Cox 1992	7/101	10/99		3.7	0.69 [0.27, 1.73]
Guibert 1997	8/212	10/209		3.9	0.79 [0.32, 1.96]
Henry 1999	42/394	46/386		14.8	0.89 [0.60, 1.33]
Hooton 1991	7/49	8/47		3.7	0.84 [0.33, 2.13]
Iravani 1999	8/239	48/474		5.7	0.33 [0.16, 0.69]
Menday 2000	11/219	5/221		3.0	2.22 [0.78, 6.28]

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Study	Three days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Stein 1987	12/109	5/100		3.2	2.20 [0.80, 6.03]
Stein 1992	11/197	18/207		5.8	0.64 [0.31, 1.32]
Subtotal (95% CI)	1678	1895		45.6	0.88 [0.60, 1.29]
Total events: 112 (Three days), 153 (5-10 days)					
Test for heterogeneity chi-square=15.38 df=8 p=0.05 I^2 =48.0%					
Test for overall effect z=0.64 p=0.5					
Total (95% CI)	3357	3616		100.0	0.81 [0.67, 0.97]
Total events: 226 (Three days), 306 (5-10 days)					
Test for heterogeneity chi-square=23.59 df=21 p=0.31 I^2 =11.0%					
Test for overall effect z=2.27 p=0.02					

Analysis 01.16. Comparison 01 Three days versus 5-10 day antibiotic therapy, Outcome 16 Skin adverse effects

Review: Duration of antibacterial treatment for uncomplicated urinary tract infection in women

Comparison: 01 Three days versus 5-10 day antibiotic therapy

Outcome: 16 Skin adverse effects

Study	Three-days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
01 Same antibiotic therapy in each group					
Gordin 1987a	0/32	3/30		2.7	0.13 [0.01, 2.49]
Gordin 1987b	1/36	1/34		2.9	0.94 [0.06, 14.51]
Gossius 1984	4/136	23/132		8.5	0.17 [0.06, 0.47]
Gossius 1985	0/50	7/64		2.8	0.08 [0.00, 1.45]
× Greenberg 1986	0/26	0/28		0.0	Not estimable
× Hansen 1981	0/102	0/119		0.0	Not estimable
Internordic 1988	6/239	12/240		8.9	0.50 [0.19, 1.32]
Marsh 1980	2/59	2/69		4.8	1.17 [0.17, 8.05]
Neringer 1992	16/228	28/235		10.9	0.59 [0.33, 1.06]
Piipo 1990	5/197	7/197		8.0	0.71 [0.23, 2.21]
Pitkajarvi 1990	3/174	2/171		5.3	1.47 [0.25, 8.71]
× Richards 1984	0/92	0/86		0.0	Not estimable

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Study	Three-days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Sandberg 1985	1/102	0/100		2.3	2.94 [0.12, 71.37]
Trienekens 1989	3/161	6/166		6.9	0.52 [0.13, 2.03]
Subtotal (95% CI)	1634	1671		63.9	0.51 [0.34, 0.77]
Total events: 41 (Three-days), 91 (5-10 days)					
Test for heterogeneity chi-square=10.98 df=10 p=0.36 I^2 =8.9%					
Test for overall effect z=3.17 p=0.002					
02 Different antibiotic therapy in each group					
Bitsch 1985	0/158	2/152		2.5	0.19 [0.01, 3.98]
Guibert 1997	5/212	2/209		5.8	2.46 [0.48, 12.56]
Henry 1999	27/394	6/386		9.4	4.41 [1.84, 10.56]
Iravani 1999	3/239	10/474		7.3	0.59 [0.17, 2.14]
Menday 2000	2/219	7/221		6.1	0.29 [0.06, 1.37]
Stein 1987	0/109	7/100		2.8	0.06 [0.00, 1.06]
Stein 1992	0/197	1/207		2.3	0.35 [0.01, 8.54]
Subtotal (95% CI)	1528	1749		36.1	0.69 [0.21, 2.28]
Total events: 37 (Three-days), 35 (5-10 days)					
Test for heterogeneity chi-square=19.87 df=6 p=0.003 I^2 =69.8%					
Test for overall effect z=0.61 p=0.5					
Total (95% CI)	3162	3420		100.0	0.62 [0.36, 1.06]
Total events: 78 (Three-days), 126 (5-10 days)					
Test for heterogeneity chi-square=37.71 df=17 p=0.003 I^2 =54.9%					
Test for overall effect z=1.75 p=0.08					

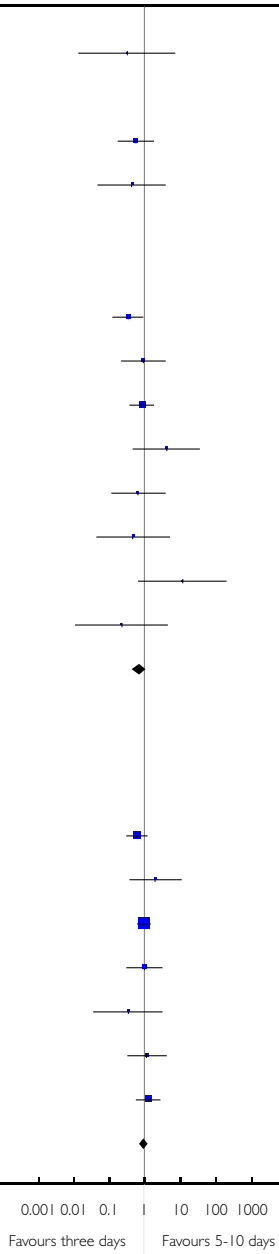
Analysis 01.17. Comparison 01 Three days versus 5-10 day antibiotic therapy, Outcome 17 CNS adverse effects

Review: Duration of antibacterial treatment for uncomplicated urinary tract infection in women

Comparison: 01 Three days versus 5-10 day antibiotic therapy

Outcome: 17 CNS adverse effects

Study	Three days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
01 Same antibiotic therapy in each group					
Gordin 1987a	0/32	1/30		0.6	0.31 [0.01, 7.40]
× Gordin 1987b	0/36	0/34		0.0	Not estimable
Gossius 1984	4/136	7/132		4.2	0.55 [0.17, 1.85]
Gossius 1985	1/50	3/64		1.2	0.43 [0.05, 3.98]
× Greenberg 1986	0/26	0/28		0.0	Not estimable
× Hansen 1981	0/102	0/119		0.0	Not estimable
Internordic 1988	5/239	15/240		6.2	0.33 [0.12, 0.91]
Marsh 1980	3/59	4/69		2.9	0.88 [0.20, 3.76]
Neringer 1992	11/228	14/235		10.4	0.81 [0.38, 1.75]
Piipo 1990	4/197	1/197		1.3	4.00 [0.45, 35.47]
Pitkajarvi 1990	2/174	3/171		1.9	0.66 [0.11, 3.87]
Richards 1984	1/92	2/86		1.1	0.47 [0.04, 5.06]
Trienekens 1989	5/161	0/166		0.7	11.34 [0.63, 203.42]
Tsugawa 1999	0/45	2/50		0.7	0.22 [0.01, 4.50]
Subtotal (95% CI)	1577	1621		31.2	0.67 [0.43, 1.04]
Total events: 36 (Three days), 52 (5-10 days)					
Test for heterogeneity chi-square=9.70 df=10 p=0.47 I^2 =0.0%					
Test for overall effect z=1.79 p=0.07					
02 Different antibiotic therapy in each group					
Cox 1992	11/101	18/99		12.6	0.60 [0.30, 1.20]
Guibert 1997	4/212	2/209		2.2	1.97 [0.37, 10.65]
Henry 1999	38/394	40/386		34.5	0.93 [0.61, 1.42]
Hooton 1991	5/49	5/47		4.5	0.96 [0.30, 3.10]
Menday 2000	1/219	3/221		1.2	0.34 [0.04, 3.21]
Stein 1987	5/109	4/100		3.7	1.15 [0.32, 4.15]
Stein 1992	13/197	11/207		10.1	1.24 [0.57, 2.71]
Subtotal (95% CI)	1281	1269		68.8	0.91 [0.68, 1.23]



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Study	Three days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Total events: 77 (Three days), 83 (5-10 days)					
Test for heterogeneity chi-square=3.69 df=6 p=0.72 I^2 =0.0%					
Test for overall effect z=0.60 p=0.5					
Total (95% CI)	2858	2890		100.0	0.83 [0.65, 1.06]
Total events: 113 (Three days), 135 (5-10 days)					
Test for heterogeneity chi-square=14.61 df=17 p=0.62 I^2 =0.0%					
Test for overall effect z=1.50 p=0.1					

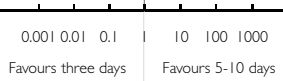
Analysis 01.18. Comparison 01 Three days versus 5-10 day antibiotic therapy, Outcome 18 Vaginal discharge as an adverse effect of therapy

Review: Duration of antibacterial treatment for uncomplicated urinary tract infection in women

Comparison: 01 Three days versus 5-10 day antibiotic therapy

Outcome: 18 Vaginal discharge as an adverse effect of therapy

Study	Three days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
01 Same antibiotic therapy in each group					
× Gordin 1987a	0/32	0/30		0.0	Not estimable
Gordin 1987b	1/36	2/34		2.9	0.47 [0.04, 4.97]
Gossius 1984	0/136	3/132		1.9	0.14 [0.01, 2.66]
× Gossius 1985	0/50	0/64		0.0	Not estimable
Greenberg 1986	0/26	1/28		1.6	0.36 [0.02, 8.42]
× Hansen 1981	0/102	0/119		0.0	Not estimable
Neringer 1992	5/228	2/235		6.1	2.58 [0.51, 13.15]
Pitkajarvi 1990	0/174	4/171		1.9	0.11 [0.01, 2.01]
Richards 1984	0/92	1/86		1.6	0.31 [0.01, 7.55]
Sandberg 1985	4/102	5/100		9.8	0.78 [0.22, 2.84]
Trienekens 1989	2/161	1/166		2.8	2.06 [0.19, 22.52]
Subtotal (95% CI)	1139	1165		28.7	0.75 [0.35, 1.59]
Total events: 12 (Three days), 19 (5-10 days)					
Test for heterogeneity chi-square=6.59 df=7 p=0.47 I^2 =0.0%					
Test for overall effect z=0.74 p=0.5					
02 Different antibiotic therapy in each group					



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Study	Three days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Cox 1992	1/101	4/99		3.4	0.25 [0.03, 2.15]
Guibert 1997	9/212	8/209		18.7	1.11 [0.44, 2.82]
Henry 1999	14/394	15/386		31.8	0.91 [0.45, 1.87]
Hooton 1991	2/49	5/47		6.4	0.38 [0.08, 1.88]
Iravani 1999	0/239	5/474		1.9	0.18 [0.01, 3.24]
Stein 1987	1/109	2/100		2.9	0.46 [0.04, 4.98]
Stein 1992	2/197	5/207		6.1	0.42 [0.08, 2.14]
Subtotal (95% CI)	1301	1522		71.3	0.73 [0.45, 1.17]
Total events: 29 (Three days), 44 (5-10 days)					
Test for heterogeneity chi-square=4.30 df=6 p=0.64 I^2 =0.0%					
Test for overall effect z=1.31 p=0.2					
Total (95% CI)	2440	2687		100.0	0.73 [0.49, 1.10]
Total events: 41 (Three days), 63 (5-10 days)					
Test for heterogeneity chi-square=10.88 df=14 p=0.70 I^2 =0.0%					
Test for overall effect z=1.51 p=0.1					

Analysis 01.19. Comparison 01 Three days versus 5-10 day antibiotic therapy, Outcome 19 Other adverse effects

Review: Duration of antibacterial treatment for uncomplicated urinary tract infection in women

Comparison: 01 Three days versus 5-10 day antibiotic therapy

Outcome: 19 Other adverse effects

Study	Three days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
01 Same antibiotic therapy in each group					
× Gordin 1987a	0/32	0/30		0.0	Not estimable
× Gordin 1987b	0/36	0/34		0.0	Not estimable
Gossius 1984	0/136	1/132		0.9	0.32 [0.01, 7.87]
Gossius 1985	0/50	1/64		0.9	0.42 [0.02, 10.21]
× Greenberg 1986	0/26	0/28		0.0	Not estimable
× Hansen 1981	0/102	0/119		0.0	Not estimable
Internordic 1988	15/239	14/240		18.3	1.08 [0.53, 2.18]

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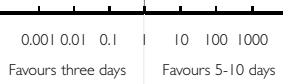
Study	Three days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Marsh 1980	3/59	2/69		3.0	1.75 [0.30, 10.15]
Neringer 1992	5/228	7/235		7.1	0.74 [0.24, 2.29]
Piipo 1990	6/197	4/197		5.9	1.50 [0.43, 5.23]
Pitkajarvi 1990	8/174	5/171		7.6	1.57 [0.52, 4.71]
Richards 1984	2/92	3/86		2.9	0.62 [0.11, 3.64]
Sandberg 1985	1/102	1/100		1.2	0.98 [0.06, 15.46]
Trienekens 1989	8/161	10/166		11.2	0.82 [0.33, 2.04]
Tsugawa 1999	2/45	0/50		1.0	5.54 [0.27, 112.47]
Subtotal (95% CI)	1679	1721		60.0	1.05 [0.71, 1.55]
Total events: 50 (Three days), 48 (5-10 days)					
Test for heterogeneity chi-square=4.16 df=10 p=0.94 I^2 =0.0%					
Test for overall effect z=0.25 p=0.8					
02 Different antibiotic therapy in each group					
Guibert 1997	18/212	18/209		23.4	0.99 [0.53, 1.84]
Henry 1999	9/394	7/386		9.6	1.26 [0.47, 3.35]
Menday 2000	3/219	9/221		5.5	0.34 [0.09, 1.23]
Stein 1987	1/109	2/100		1.6	0.46 [0.04, 4.98]
Subtotal (95% CI)	934	916		40.0	0.87 [0.53, 1.42]
Total events: 31 (Three days), 36 (5-10 days)					
Test for heterogeneity chi-square=3.07 df=3 p=0.38 I^2 =2.3%					
Test for overall effect z=0.55 p=0.6					
Total (95% CI)	2613	2637		100.0	0.98 [0.72, 1.32]
Total events: 81 (Three days), 84 (5-10 days)					
Test for heterogeneity chi-square=7.56 df=14 p=0.91 I^2 =0.0%					
Test for overall effect z=0.15 p=0.9					



Analysis 01.20. Comparison 01 Three days versus 5-10 day antibiotic therapy, Outcome 20 Patients with any adverse effects during treatment by antibiotic class (same drug)

Review: Duration of antibacterial treatment for uncomplicated urinary tract infection in women

Comparison: 01 Three days versus 5-10 day antibiotic therapy

Outcome: 20 Patients with any adverse effects during treatment by antibiotic class (same drug)

Study	Three days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
01 Quinolones					
Internordic 1988	46/239	58/240		13.3	0.80 [0.57, 1.12]
Neringer 1992	57/228	73/235		15.1	0.80 [0.60, 1.08]
Piipo 1990	28/197	22/197		8.4	1.27 [0.75, 2.15]
Trienekens 1993	26/199	29/193		9.1	0.87 [0.53, 1.42]
Tsugawa 1999	4/45	5/50		2.1	0.89 [0.25, 3.11]
Subtotal (95% CI)	908	915		48.0	0.86 [0.72, 1.04]
Total events: 161 (Three days), 187 (5-10 days)					
Test for heterogeneity chi-square=2.56 df=4 p=0.63 I^2 =0.0%					
Test for overall effect z=1.55 p=0.1					
02 Beta-lactams					
Gordin 1987b	2/36	3/34		1.1	0.63 [0.11, 3.54]
Greenberg 1986	0/26	1/28		0.4	0.36 [0.02, 8.42]
Hansen 1981	3/102	7/119		1.9	0.50 [0.13, 1.88]
Hovelius 1985	2/27	1/33		0.6	2.44 [0.23, 25.53]
Marsh 1980	17/59	22/69		8.3	0.90 [0.53, 1.53]
Pitkajarvi 1990	21/174	20/171		7.4	1.03 [0.58, 1.83]
Richards 1984	8/92	15/86		4.4	0.50 [0.22, 1.12]
Sandberg 1985	10/102	12/100		4.6	0.82 [0.37, 1.80]
Subtotal (95% CI)	618	640		28.7	0.82 [0.61, 1.11]
Total events: 63 (Three days), 81 (5-10 days)					
Test for heterogeneity chi-square=3.94 df=7 p=0.79 I^2 =0.0%					
Test for overall effect z=1.28 p=0.2					
03 TMP/sulfonamides					
Gordin 1987a	0/32	5/30		0.4	0.09 [0.00, 1.48]
Gossius 1984	12/136	37/132		6.9	0.31 [0.17, 0.58]
Gossius 1985	4/50	18/64		3.0	0.28 [0.10, 0.79]
Trienekens 1989	40/161	51/166		13.0	0.81 [0.57, 1.15]
Subtotal (95% CI)	379	392		23.3	0.40 [0.19, 0.88]

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Study	Three days n/N	5-10 days n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Total events: 56 (Three days), 111 (5-10 days)					
Test for heterogeneity chi-square=11.44 df=3 p=0.010 I^2 =73.8%					
Test for overall effect z=2.30 p=0.02					
Total (95% CI)	1905	1947		100.0	0.76 [0.63, 0.92]
Total events: 280 (Three days), 379 (5-10 days)					
Test for heterogeneity chi-square=22.63 df=16 p=0.12 I^2 =29.3%					
Test for overall effect z=2.87 p=0.004